A STUDY ON INCIDENCE AND ETIOLOGY OF HYPONATREMIA IN HOSPITALISED PATIENTS

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations

for the award of the degree of

GENERAL MEDICINE

M.D. BRANCH – I

MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL, CHENNAI – 3

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA

MARCH 2010

CERTIFICATE

This is to certify that the dissertation titled **"A STUDY ON INCIDENCE AND ETIOLOGY OF HYPONATREMIA IN HOSPITALISED PATIENTS"** is the bonafide original work of **Dr. KRISHNA SHANKAR. G** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2010. The Period of study was from January 2008 to June 2009.

Dr.R. SUKUMAR, M.D.,
Professor of Medicine
Institute of Internal Medicine
Madras Medical College
Chennai-600 003

Dr.C.RAJENDIRAN, M.D.
Director & Professor
Institute of InternalMedicine
Madras Medical College
Chennai-600 003

Dr. J. MOHANASUNDARAM, M.D., Ph.D., DNB
D E A N
Madras Medical College and Government General Hospital
Chennai – 600 003

DECLARATION

I, **Dr.KRISHNA SHANKAR, G.** solemnly declare that dissertation titled **"A STUDY ON INCIDENCE AND ETIOLOGY OF HYPONATREMIA IN HOSPITALISED PATIENTS"** is a bonafide work done by me at Madras Medical College and Government General Hospital, Chennai, during January 2008 to June 2009 under the guidance and supervision of **Prof. R.Sukumar, M.D.,** Professor of Medicine, Madras Medical College and Government General Hospital, Chennai.

This dissertation is submitted to the Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

Pla

ce : Chennai **(Dr. KRISHNA SHANKAR. G)**

Date :

ACKNOWLEDGEMENT

My sincere thanks to **Prof.Dr.J.Mohanasundaram M.D., DNB., Ph.D.**, Dean, Madras Medical College and Government General Hospital, Chennai, for granting me permission to conduct this study and for providing me with all the necessary help during the period of my study.

I am extremely grateful to **Prof.Dr.C.Rajendiran M.D.,** Director and Head of the Institute of Internal Medicine, Government General Hospital, Chennai, for his full fledged support throughout my study and valuable suggestions and guidance during my study and my post graduate period.

I am greatly indebted to **Prof.Dr.R.Sukumar.M.D.,** my Professor and Unit Chief, who is my Guide in this study, for his timely suggestions, constant encouragement and scholarly guidance in my study and post graduate period.

My sincere thanks to Assistant Professors **Dr.R.S.A.Alexander.M.D., DCH** and **Dr.S.Deepa, M.D.,** for their motivation, encouragement and support.

I express my sincere thanks to **Prof.Dr.Pragna Dohlia, M.D.,** Director and Head of Institute of Biochemistry, Government General Hospital, Chennai, for her support in utilizating Laboratory services and valuable guidance in the study.

A special mention of thanks to all the patients who participated in this study for their kind cooperation.

I would like to thank my colleagues and friends who have been a constant source of encouragement.

CONTENTS

INTRODUCTION

Hyponatremia is the most common electrolyte disorder among hospitalized patients and has been associated with increased mortality. Hyponatremia is defined as a serum sodium concentration (Na^+) less than 135 mEq/L.

Serum sodium levels and serum osmolality are normally maintained under precise control by homeostatic mechanisms involving thirst, anti-diuretic hormone and the renal handling of filtered sodium. Hyponatremia occurs in a broad spectrum of patients who are asymptomatic or critically ill.

Patients in whom the serum sodium concentration is greater than 130 mEq/L are usually asymptomatic, whereas those in whom these values are lower may have symptoms. Clinical symptoms vary from individual to individual. Majority of patients with hyponatremia are asymptomatic. Most patients with hyponatremia have non-specific symptoms or symptoms due to an underlying disease or disorder. The clinical manifestations of hyponatremia are produced by brain swelling and are primarily a function of the rate of fall of serum sodium concentration and not the absolute level. Symptoms occurring early in hyponatremia is usually anorexia, nausea, vomiting. Some patients may have headache and irritability. As serum sodium levels falls further patients develop neuropsychiatry symptoms.

These symptoms range from restlessness, altered consciousness, lethargy, seizures to coma. As the symptomatology vary markedly, the diagnosis of hyponatremia is difficult to establish. Prompt recognition and optimal management of hyponatremia in hospitalized patients may reduce in-hospital mortality and symptom severity, allow for less intensive hospital care, decrease the duration of hospitalization and associated costs and improve the treatment of underlying co morbid conditions and patients' quality of life. So the treating clinician should have a high index of suspicion to diagnose hyponatremia.

There are serious neurological sequelae associated with hyponatremia and its management. The possible causes of hyponatremia should always be sought in every case. The presence of symptoms and duration of hyponatremia guide the treatment strategy. Thorough evaluation for hyponatremia mandates accurate history taking and clinical examination along with various investigations.

AIMS AND OBJECTIVES OF THE STUDY

- To study the incidence of hyponatremia in hospitalized adult patients in medical wards.
- To determine the etiology of clinically significant hyponatremia in 100 patients in medical wards.
- To determine the clinical presentation of hyponatremia in these patients.
- To study whether the primary disease is a cause for hyponatremia and whether other features cause hyponatremia also.
- To study whether hyponatremia adds to morbidity and mortality.
- To study the various diseases associated with hyponatremia.

REVIEW OF LITERATURE

INCIDENCE

Hyponatremia is common in both inpatients and outpatients[1].It is the most common electrolyte disorder among hospitalized patients[2,3,4,] and has been associated with increased mortality[5] ranging from 5% to 50%, depending on severity and acuity of onset[6]. Its prevalence among non-hospitalized elderly patients has been estimated to be between 7 – 11.4%, increasing to 11 – 22.5% among hospitalized patients[7]. The precise incidence of hyponatremia varies depending on the conditions underlying it and the criteria used to define it. When defined as a serum sodium concentration of less than 135 mEq/L, hyponatremia has been reported in 15% to 22% of hospitalized patients. In studies defining it as a concentration of 130 mEq/L or less, hyponatremia has been described in hospitalized patients at incidences of 1% to 4%[8,9] and a prevalence of 2.9%[10]. A study done by Kende M et al in over 30,000 patients over two years observed that hyponatremia was higher among medical and pediatric patients[11]. Various studies have indicated that elderly patients showed a higher predisposition to develop hyponatremia[12,13]. Natkunam et al observed that majority of patients developed hyponatremia during their hospital stay[14]. Various studies have emphasized the susceptibilities of hospitalized elderly patients to hyponatremia[15,16].

Studies have shown that elderly patients are more prone to hyponatremia as a result of conditions such as cardiac, renal and hepatic failure[15,17], physiological changes such as a decrease in glomerular filtration rate,[18,19] altered water metabolism[20] and polypharmacy[21]. Hyponatremia in elderly in-patients is common during in-hospital stay is strongly associated with increased length of stay and loss of independence[22].

PHYSIOLOGY OF SODIUM AND FLUID BALANCE

Sodium is the predominant cation in extra-cellular fluids[16]. The molecular weight of sodium is 23 and valency is 1+. Osmolality is the total number of solute particles dissolved in a given volume of solvent. It is measured by number of milli-osmoles of solutes dissolved in one Kg per liter of water. The dissociability of particular solute determines its contribution to osmolality.

Plasma osmolality can be calculated using the following formula:

Mosm/kg = 2(Na^+ mmol/L) + glucose (mg/dl)/18 + urea (mg/dl)/6[23]

Physiology of Osmosis

Cell membranes throughout the body are freely permeable to water but are impermeable to various solutes. Osmotic fluid movement occurs when such a water permeable membrane separates two compartments with different concentrations of impermeable solutes. The difference between the osmolality on the two sides is called the osmotic gradient. Osmotic gradient determines the

amount of fluid that will passively move to equalize the osmolality on the two sides.

Most body fluids are iso-osmotic with plasma or cell interior. In a few places, high osmotic gradients are maintained as seen in renal medulla. This is made possible by specialized water impermeable membranes.

COMPOSITION OF VARIOUS FLUID COMPARTMENTS

The total body water is about 54 percent of body weight in normal individual. 15 – 20 percent may comprise the extra-cellular fluid, which includes plasma and interstitial fluid[24].

Table 1

VOLUMES OF BODY FLUID COMPARTMENTS		
TOTAL BODY WATER	40L	
INTRA-CELLULAR VOLUME	24L	60%
PLASMA	3.2L	8%
INTERSTITIAL FLUID	11.2L	28%
TRANSCELLULAR FLUID	1.6L	4%
A NORMAL MAN WEIGHING 70 KG USED AS MODEL		

The total body water is measured by various dilution techniques using isotopes like deuterium or tritium.

Table 2

VOLUME AND COMPOSITION OF BODY FLUIDS			
Measure	**Intra-cellular**	**Extra-cellular**	
		Plasma	**Interstitial**
Water ml/kg	400 (330 – 450)	50 (45 – 35)	150 (120 – 220)
CATIONS m mol/L			
Na	3	140 135(-145)	135 (130 – 140)
K	140(120 – 160)	4.5 (3.5 – 5.0)	4.5(3.5 – 4.5)
Ca	2(1.5 – 2.5)	2.5 (2 – 3)	1.5 (1 – 2)
Mg	15(12 – 17)	2.0	1.5
ANIONS m mol/L			
Cl	6 (4 – 9)	103 (95 – 110)	108 (100 – 115)
HCO_3	8 (6 – 10)	26 (22 – 30)	27 (22 – 30)
PHOSPHATES		2	2
SULPHATES		2	2
ORGANIC ACIDS	16	3	3
ORGANIC PHOSPHATES	75		
OTHER m mol/L			
UREA		4	4
GLUCOSE	4	5 (4 – 6)	5 (4 – 6)
OSMOLALITY (m Osm/L)	287 (280 – 295)	287 (280 – 295)	287 (280 – 295)

As evident from table-2, the body fluids are in osmotic equilibrium. Various control mechanisms acting through osmo-receptors function to maintain the osmolalaity in a very narrow range. The volume of extra-cellular fluid is maintained by reflex mechanisms through volume receptors to maintain circulating volume.

REGULATION OF SODIUM AND WATER BALANCE

Sodium is the dominant cation in extra-cellular fluid and total body sodium balance is primary determinant of extra-cellular fluid volume. Hyponatremia represents a state where there is excess of water with respect to

sodium. Both water and sodium are in a state of exchange with the environment as show in the table-3[24].

Table 3

SODIUM AND WATER BALANCE IN A NORMAL INDIVIDUAL					
Source	Water intake		Source	Water output	
	Obligatory	Elective		Obligataory	Elective
INGESTED	400	1000	URINE	500	1000
CONTENT IN FOOD	850		SKIN	500	
OXIDATION	350		STOOL	200	
			RESPIRATIOAN	400	
TOTAL	1600	1000		1600	1000
	Sodium Intake (m mol / Kg / day)			Sodium output (m mil / Kg / day)	
DIETARY	1.0		URINE	2.6	
INCIDENTAL	1.9		FAECES	0.1	
			INSENSIBLE	0.2	
TOTAL	2.9			2.09	

The normal plasma osmolality is 275 – 290 m Osm/kg. The normal plasma sodium is 135 -145 mEq/L. The plasma osmolality is chiefly determined by plasma sodium concentration. The osmolality is normally maintained within narrow limits by appropriate variations in water intake and excretion. This is governed by osmo-receptors in the hypothalamus which influences both thirst and ADH secretion.

THIRST

Thirst is a subjective sensation that culminates in drinking. Thirst may be triggered by osmotic and non-osmotic stimuli.

Osmotic regulation of thirst

The osmo-receptors for the thirst are situated in anterolateral hypothalamus, close to the receptors that regulate AVP release[25]. Changes in tonicity (effective osmolality) stimulate thirst. When tonicity exceeds 290 m Osm/kg, thirst first appears. This threshold is about 10 m Osm higher than that for vasopressin release.. Stimulus for thirst is slightly blunted in elderly.

Non-osmotic regulation of thirst

Non-osmotic stimuli for thirst include social practices, pharyngeal dryness or decrease in volume of extra-cellular fluid independent to alteration of tonicity of extra-cellular fluid. Decreases in extra-cellular fluid volume stimulate thirst via rennin-angiotensin system. Angiotensin-II acts as a probable mediator by its dipsogenic effect[25, 28]. Other dipsogens include antidepressants, β-adrenergic and cholinergic agents.

In elderly person, there is blunted thirst response to hyper-osmolality resulting in hypernatermia. Psychogenic polydipsia may be seen in psychiatric patients.

Anti-diuretic Hormone, Arginine Vasopressin

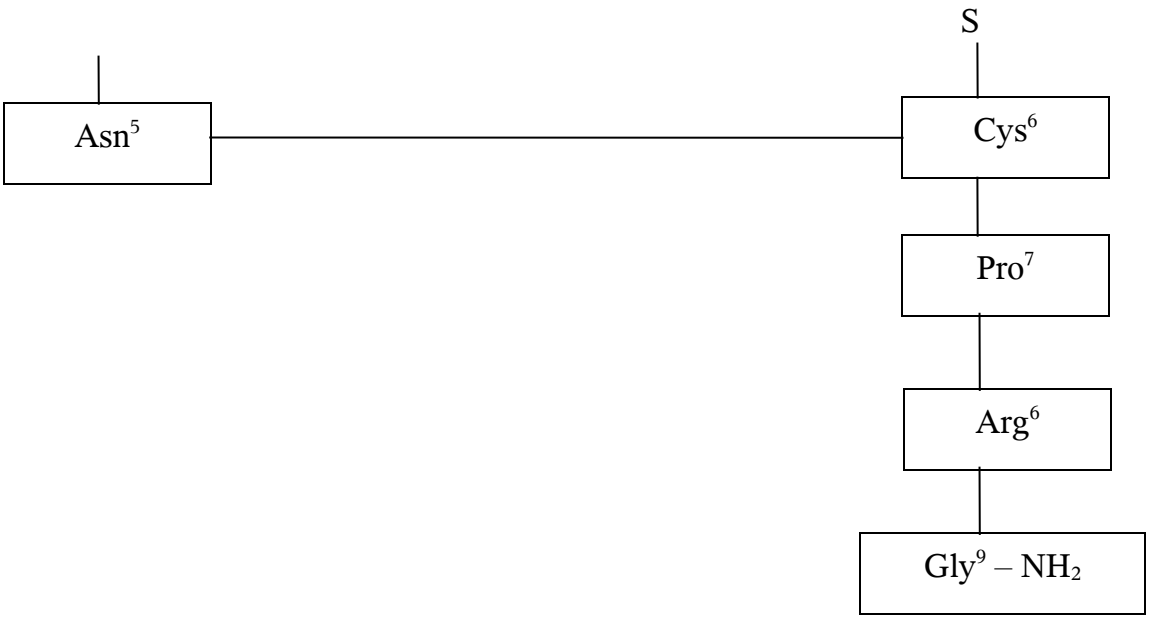
Arginine Vasopressin (AVP) is a non-peptide synthesized in supra-optic and para-ventricular nuclei of hypothalamus. It moves via neutral axons to posterior pituitary where it is stored as granules and released in response to stimulus[29]. The pro-hormone is called pro-pressophysin and it is proteolysed in posterior pituitary to AVP. It plays a pivotal role in water homeostasis by its action on most distal segment of the nephron.

Structure of AVP

AVP is a nona-peptide. The presence of basic amino acid arginine is crucial for anti-diuresis. The secretory process involves extrusion by exocytosis coupled to cellular uptake of calcium.

Figure 1

Struture of human AVP



Release of AVP

Vasopressin is released from posterior pituitary in response to osmotic and non-osmotic stimuli. The plasma level of AVP detected by radio-immunoassay is about 2.5 pg/ml at normal plasma osmolality of 285 m Osm/kg[25].

Osmotic regulation of Vasopressin

Osmo-receptors for AVP release are in hypothalamus close to receptors for thirst. These osmo-receptors are more sensitive to change in osmolality. A change of osmolality of even one percent of normal osmolality brings about significant change in circulating AVP levels[25, 27].

AVP is suppressed below plasma osmolality of 280 m Osm/kg. With fall in levels of AVP kidneys produce maximally dilute urine. When osmolality

rises, plasma AVP levels rise in a linear fashion causing production of concentrated urine.

Factors affecting osmotic threshold for vasopressin release are nature of osmotic particle, genetics, age, intravascular volume and drugs. Urea is permeable and has no effect. In absence of insulin, glucose is impermeable and may exert an osmotic effect. Ageing, hypocalcaemia and lithium increase the sensitivity of osmo-receptors whereas tegretol, pregnancy slightly decrease its sensitivity[29].

Non-osmotic regulation of vasopressin

Decrement in pressure or plasma volume causes prompt secretion of AVP. Non osmotic regulation requires a change of up to 7 – 10%[30, 31]. But once non-osmotic release of ADH has been started, it overrides the osmotic modulation. By this mechanism, there will be continued secretion of ADH in hypovolemia. Non osmotic stimuli trigger ADH release through volume and baro-receptors located in aortic arch, carotid sinus and atria connected via para-sympathetic afferentS[30,31]. Other stimuli like nausea, pain, stress, hypoxia, drugs[32, 33] can stimulate ADH secretion[34].

Renal regulation of water excretion

Nephron is the functional unit of kidney. It is composed of glomerulus, proximal tubule, loop of Henle, distal convoluted tubule and collecting duct.

Blood is filtered in the glomerulus producing ultra filtrate at the rate of 100 – 125 ml/min. This is known as glomerular filtration rate.

In the proximal convoluted tubule 70% is reabsorbed passively. This does not contribute to water regulation which is done in the remainder of nephron.

The loop of Henle, which is in juxta-position with vasa recta enable nephron to produce hypotonic tubular fluid with hypertonic interstitium with potential for formation of concentrated urine. The loop of Henle and vasa recta have a counter current design and fluids flow in opposite directions. The loop of Henle is a countercurrent multiplier, which relies on energy dependent transport and formation osmotic gradient.

The descending limb is permeable to solutes and water, allowing water to move outward into the hypertonic interstitium. The entry of solutes into the descending limb from interstitium is by simple osmotic forces. The ascending limb is impermeable to water and in thick ascending limb, there is co-transport of sodium, potassium and chloride. The combination of impermeability of water and outward movement of solutes produces a hypotonic fluid in tubule and hypertonic interstitium and created the gradient for countercurrent multiplier. The vasa recta by removal of water and preventing loss of solute maintain the hypertonic intersititum.

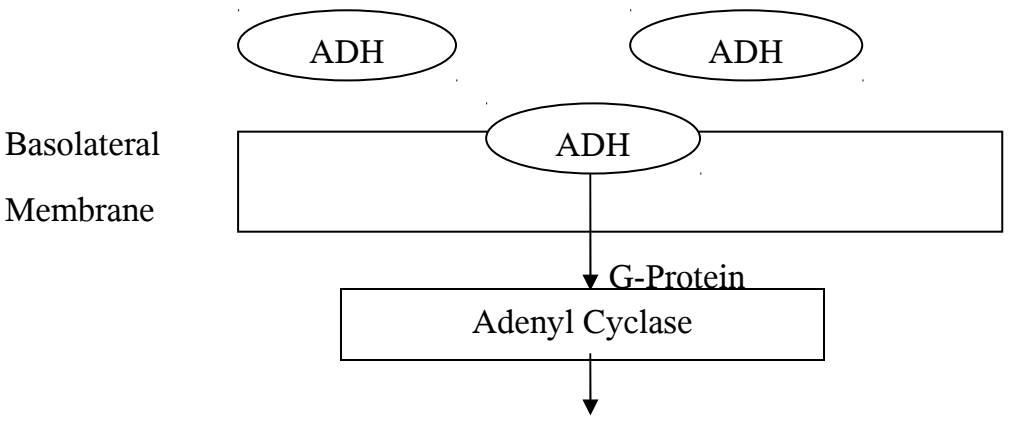
The fluid in distal convoluted tubule is always hypotonic regardless of the tonicity of final urine. Another important site of water regulation is collecting ducts. In absence of ADH, the collecting ducts are impermeable to water and

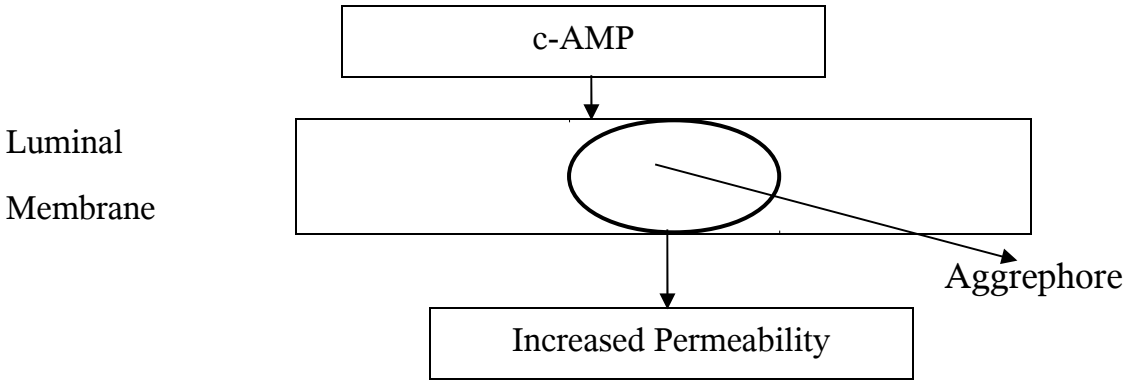
hence osmotic equilibration between tubular fluid and hypertonic interstitium does not occur, resulting in maximally dilute urine. In the presence of ADH, collecting duct becomes highly permeable to water and osmotic equilibration producing concentrated urine. The collecting ducts ultimately determine whether the kidney is producing dilute or concentrated urine.

Mechanism of action of vasopressin

Vasopressin binds to specific receptor on baso-lateral membrane of collecting duct epithelial cells. A pair of G-protein receptors causes an increase in cyclic AMP level. This stimulates protein kinase which causes intra-membranous particles to aggregate. These particles are called as aggrephores and act as water channels to increase permeability[26].

Figure – 2





To summarize, excretion of maximally dilute (<100mOsm/kg) urine,concentrated(1200mOsm/kg) urine requires an adequate GFR and delivery of fluid to functioning distal sites and functioning of ADH.

PATHOPHYSIOLOGY OF HYPONATREMIA

Sodium is the major osmotically active extra-cellular cation. Under normal circumstances, the body regulates plasma sodium concentration by adjusting the water content in ECF. Despite wide fluctuations in water and sodium intake, the plasma concentration of sodium is maintained within normal range. The integrated role of thirst, vasopressin and renal response maintain this tight balance between sodium and water[33,34,35]. Therefore, hyponatremia is almost always due to a defect in water balance.The kidneys play a key role in water homeostasis[36] by the countercurrent mechanism[38].

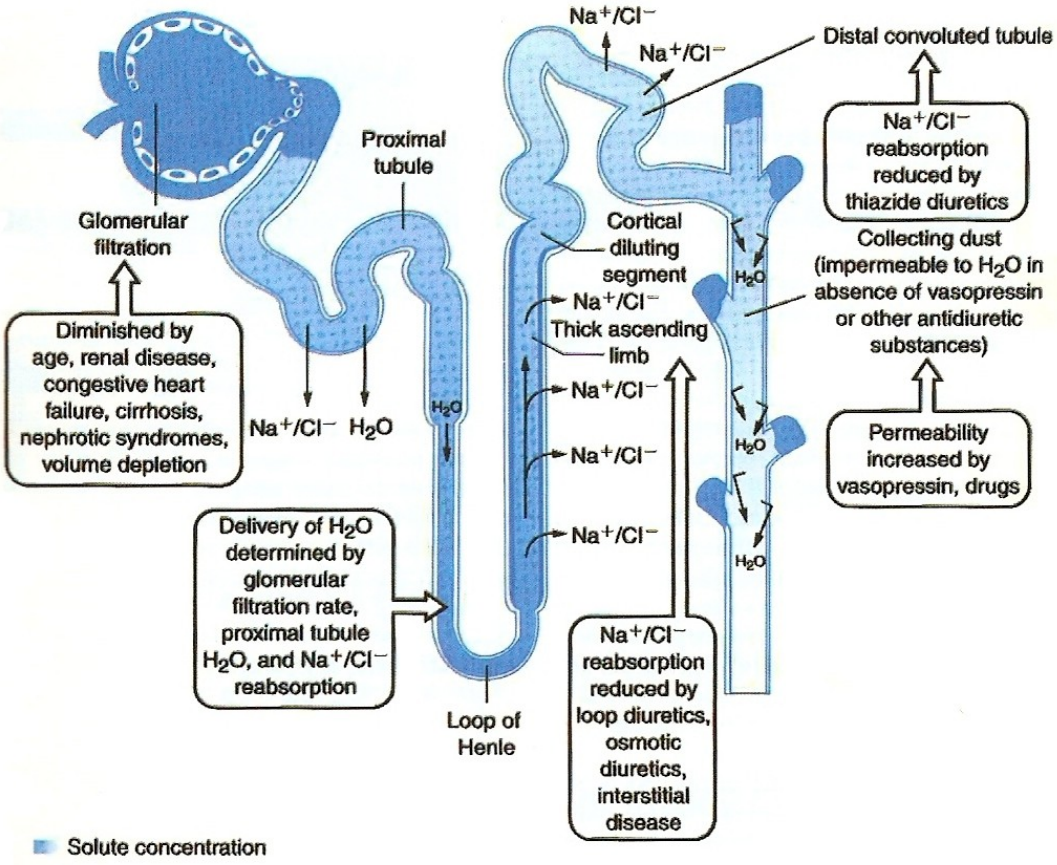
The distal convoluted tubule which is relatively impermeable to water, does active reabsorption of sodium. The collecting duct is the site of osmotic equilibration, which is mediated by vasopressin. Water channels called aquaporins, in the collecting duct cells facilitate the rapid transport of water

across cell membranes[39]. Ten separate aquaporins have been identified so far, and at least six are known to be present in the kidney along the nephron and collecting duct[40,41]. Aquaporin-2 has been shown to be a vasopressin dependent water channel controlling collecting duct water permeability[42]. The binding of arginine vasopressin to its V2 receptor in the collecting duct principal cell initiates cAMP-mediated phosphorylation of the aquaporin-2 water channel. This results in translocation of aquaporin-2 containing vesicles from their cytosolic location to the apical membrane of the collecting duct, thereby allowing the passive movement of water from tubule fluid to medullary interstitium along the osmotic gradient crerated by the countercurrent concentrating mechanism[43]. The mineralocorticoid Aldosterone also increases net sodium re-absorption through its action on the collecting tubules. Atrial natriuretic peptide inhibits sodium re-absorption , causing natriuresis and diuresis[44]. Glucocorticoids[45], glucagon[46], calcitonin[47] and prostaglandins[48] may all modify the effect of vasopressin at the renal tubular level.

Pathogenesis of hyponatremia

The normal components of the renal diluting mechanism are depicted in Figure-3[49]. Hyponatremia results from disorder of this diluting capacity of the kidney in the following situations.

Figure 3



1. Intra-renal factors such as a diminished GFR or an increase in proximal tubule fluid and sodium re-absorption can decrease distal delivery to the diluting segments of the nephron. This is seen in volume depletion, congestive heart failure, cirrhosis or nephrotic syndrome.

2. A defect in sodium chloride transport out of the water impermeable thick ascending limb of the loop of Henle occurs in patients with interstitial renal disease or in patients on diuretics.

3. Continued secretion of ADH despite the presence of serum hypo-osmolality mostly stimulated by a non-osmotic mechanism.

Classification of Hyponatremia

A very practical approach is to classify hyponatremia on the basis of ECF volume status into hypovolumic, euvolumic or hypervolumic hyponatremia[50,51]. This classification is useful in making an appropriate diagnosis and designing effective treatment of hyponatremia.

Pseudo-hyponatremia

Pseudo-hyponatremia is an artificial reduction in plasma sodium concentration in the presence of marked elevation of plasma proteins or lipids. Measurement of plasma sodium with ion-specific electrodes instead of flame photometry may alleviate this problem[52,53].

Hypovolumic hyponatremia

Loss of both sodium and water either through the kidneys, gastrointestinal tract or skin can lead to ECF volume depletion. The resultant hypovolumia stimulates vasopressin secretion, impairing renal free-water excretion. In this

setting, excessive oral or parenteral hypotonic fluid intake can lead to water retention and eventual hyponatremia. Hyponatremia is a common complication of diuretic therapy. Thiazide diuretics are the commonest cause of hypovolumic hyponatremia. Besides hypovolumia, thiazide diuretics may precipitate polydipsia along with decreased urinary dilutional capacity, as shown by Freidman et al[54]. Hyponatremia secondary to diuretics is multi-factorial. Excessive renal sodium loss, vasopressin stimulation and potassium depletion are the most important mechanisms. Hyponatremia due to thiazides is generally seen within two weeks of initiating therapy[56]. The presence of hyponatremia, hypokalemia, metabolic alkalosis, hypomagnesaemia and increased fractional excretion of potassium is suggestive of diuretic induced hyponatremia.

In adrenal insufficiency, salt depletion is due to excessive urinary sodium loss from aldosterone deficiency, which causes a reduction of intravascular volume that stimulates vasopressin secretion through baro-regulatory mechanisms[57]. A further increase in vasopressin secretion results from gluco-corticoid deficiency.

In an intensive care setting, cerebral salt wasting syndrome is not uncommon. First described by Peters et al[58], this entity was eclipsed by the syndrome of inappropriate anti-diuretic hormone secretion. There is evidence to indicate that cerebral salt wasting syndrome is seen in many patients with intracranial disease such as stroke, head injury, sub-arachnoid hemorrhage,

cerebral tumors. Cerebral salt wasting syndrome is characterized by hyponatremia, hypovolumia, natriuresis and dieresis[59]. The mechanism by which intracranial disease leads to cerebral salt wasting syndrome is not well understood. The postulated mechanism include disruption of neural input into the kidney or the central elaboration of a circulating natriuretic factor or both[59,60]. Cerebral salt wasting syndrome usually resolves spontaneously within two or three weeks of cerebral insult and responds well to prompt treatment with intravenous saline[61].

Euvolumic Hyponatremia

In euvolumic hyponatremia, the body water content is increased with a normal to mild decrease in total body sodium. In most cases of euvolumic hyponatremia, the intravascular volume is normal. Post-surgical hyponatremia is frequently seen in hospitalized patients and it is iatrogenically induced by inappropriate hypotonic fluid replacements. Elevated levels of vasopressin in the post-operative period prevent free-water excretion, resulting in hyponatremia. Euvolumic hyponatremia can be due to translocation hyponatremia, SIADH, hypothyroidism, adreno-corticotropin deficiency or primary polydipsia.

Translocation hyponatremia

It results from a shift of water from cells to the ECF that is driven by solutes confined in the extracellular compartment[62]. It occurs with glucose, mannitol[50], sorbitol, glycerol and radio-contrast agents and is called translocation

hyponatremia. Poor glycemic control accounts for hyponatremia in 10% to 20% of the hospitalized patients[9]. Hillier et al proposed a correction factor of 2.4 mEq/L decrease in sodium concentration per 100 mg/dl increase in glucose concentration[63]. This factor is better than the usual correction factor of 1.6 in mEq/L. Translocational hyponatremia is seen following transurethral resection of prostate and endoscopic uterine surgeries. It is mainly due to absorption of irrigating fluids used during this procedures[64,65].

Syndrome of inappropriate anti-diuretic hormone secretion

SIADH is an important cause of hyponatremia that occurs when normal control of secretion is lost and ADH is secreted independently of the body's need to conserve water. ADH causes water retention, so hyponatremia then occurs as a result of inappropriately increased water retention in the presence of sodium loss[51]. The hyponatremia in SIADH secretion results from either increased circulating vasopressin as seen in lung malignancies or from abnormal osmo-regulation from a 'reset osmostat' for vasopressin secretion, such that vasopressin is released at an abnormally low threshold of plasma osmolality[66,67]. Another important factor that leads to hyponatremia in patients with SIADH is the abnormal increase in thirst[68]. Patients with SIADH continue to drink normal amounts of fluid, despite plasma osmolalities well below the physiological osmotic threshold for onset of thirst. There is downward resetting of the osmotic threshold for thirst in SIADH[69].

Causes of syndrome of Inappropriate Anti-diuretic Hormone Secretion[35]

Central nervous system disorders

- Vascular diseases (thrombosis, embolism, hemorrhage, vasculitis), trauma (subdural hematoma, subarachnoid or intracranial hemorrhage), tumor, hydrocephalus, infection (meningitis, encephalitis, brain abscess),Acute intermittent porphyria, Systemic Lupus erythematosus, Postoperative transsphenoidal hypophysectomy, Schizophrenia

Neoplasms with ectopic hormone production

- Small-cell carcinoma of the lung, Pharyngeal carcinoma, Pancreatic carcinoma, Thymoma, Lymphoma, Hodgkin's disease, reticulum cell sarcoma, Bladder carcinoma

Pulmonary disease

- Pneumonia, Lung abscess, Bronchiectasis, Tuberculosis

- Endocrine disease
  - Pituitary tumor, Hypothyroidism, Adrenal insufficiency

- Others
  - Positive pressure ventilation, Acquired Immune Deficiency syndrome, Idiopathic SIADH of the elderly, Nausea, pain, psychosis

SIADH is diagnosed by following criteria

Essential criteria

1. Hypo-osmolality (plasma osmolality <270 m Osm/kg).
2. Inappropriately concentrated urine (>100 m Osm/kg).
3. Clinical euvolumia.
4. Elevated urine sodium (>40 mEq/L) with normal salt and water intake.
5. Euvolumia with normal adrenal, thyroid, renal and liver functions.

Supplemental criteria

1. Abnormal water load test. (Inability to excrete at least 90% of a 20 mL/kg water load in 4 hrs or failure to dilute urinary osmolality to <100 m Osm/kg).
2. Plasma anti-diuretic hormone level inappropriately elevated relative to plasma osmolality.
3. No significant correction of plasma sodium with volume expansion, but improvement after fluid restriction.

Hypothyroidism

The pathophysiology of hyponatremia in hypothyroidism is still unclear, as both increased total body sodium and increased plasma vasopressin levels have been reported[70].Reduced stroke volume stimulates vasopressin release[71].

Decreased free-water excretion is suggested and supported by data from water loading studies in hypothyroid patients[70].

Adreno-corticotrophin deficiency

Increased plasma levels of vasopressin have been shown in adreno-corticotrophin deficient patients presenting with hyponatremia[72] and there is evidence to suggest impaired free-water excretion[73].

Primary polydipsia

Psychogenic polydipsia frequently seen in psychiatric patients is secondary to excessive water intake[74]. Plasma levels of arginine-vasopressin are partially suppressed in these patients[75]. The dilutional ability of the kidney is overwhelmed by excessive water intake. In patients who consume excessive amounts of beer, this is further exaggerated by poor caloric intake.

Hypervolumic hyponatremia

It is characterized by clinical evidence of volume overload with peripheral edema in heart failure and cirrhosis. There is an excess of total body sodium and water[76]. A decrease in mean arterial pressure leads to resultant secondary hyper-aldosteronism which causes increased distal renal tubular sodium re-absorption and subsequent increase in total body sodium.

Simultaneously, there is a failure of normal physiologic escape from the anti-natriuretic effect of aldosterone[78]. Thus, increase in total body water results from increased vasopressin concentration, causing up-regulation at aquaporin2 water channels and further anti-diuresis[79].

Cerebral adaptation to hyponatremia

When the extra-cellular osmolality falls water starts to move into the cells. This increases the intracellular volume and result in tissue edema. This cellular edema when occur within the fixed confines of the cranium, it causes increased intracranial pressure, leading to neurological symptoms. To prevent this, mechanisms of volume regulation come into operation in patients with hyponatremia. After induction of extra cellular fluid hypo-osmolality, free water moves into the brain in response to osmotic gradients, producing cerebral edema (bottom panel). However, within one to three hours, a decrease in cerebral extra-cellular volume occurs by movement of fluid into the cerebrospinal fluid, which is then shunted back into the systemic circulation. This happens very promptly and is evident by the loss of extra-cellular and intracellular solutes as early as half an hour after the onset of hyponatremia. As the loss of water accompany the loss of brain solute (middle panel) the expanded brain volume decreases back towards normal (upper panel).

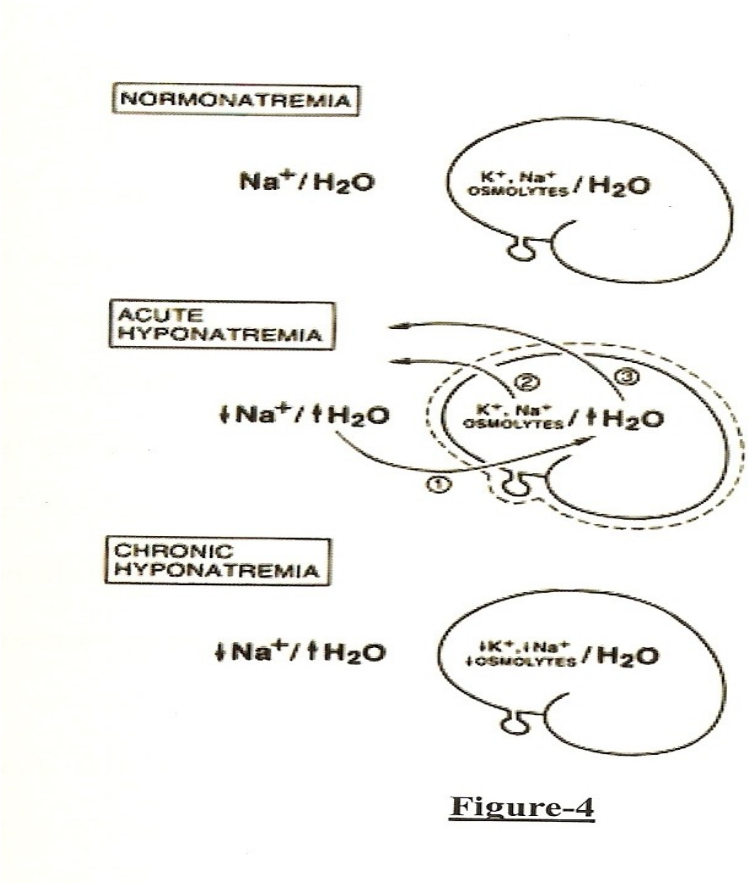


Figure-4

CLINICAL FEATURES

Clinical symptoms of hyponatremia vary from individual to individual[49]. Hyponatremia is defined as a serum sodium concentration less than 135 mEq/L[7, 8, 50,51,80,81,82,83,84].

Hyponatremia is not a disease in itself ,[85]it is frequently a marker of significant underlying disease[86]. Patients in whom the serum sodium concentration is greater than 130 mEq/L are usually asymptomatic. The severity of symptoms increase with the degree of fall in serum sodium level and rapidity with which the fall occurs[89]. Several factors other than fall in serum sodium contribute to the symptomatology like extremes of age, female sex, underlying systemic diseases . Patients in hypoxia, acidosis and hypercapnia may be more

symptomatic[49]. Initially symptoms of hyponatremia are gastrointestinal symptoms. Symptoms occurring early in hyponatremia are usually anorexia, nausea and vomiting. Some patients may have headache and irritability. As serum sodium level falls further patients develop neuropsychiatric symptoms. These symptoms range from restlessness, altered consciousness, gait disturbances, lethargy, obtundation, myoclonic jerks, seizures, status epilepticus to coma[49,90,91,92,93]. Some patients may develop muscle cramps and weakness on exertion[94]. Severe and rapidly evolving hyponatremia may present with seizures, coma, permanent brain damage, respiratory arrest, brainstem herniation and death[88]. Hyponatremia is a major cause of brain damage, dementia and death among hospitalized patients and its coexistence with other major medical illnesses (heart failure, myocardial infarction, tuberculosis, cirrhosis) increase overall in-hospital mortality by at least six fold[95].

The symptoms vary with acute and chronic hyponatremia. When serum sodium falls gradually, over a period of several days or weeks, patients will have minimal symptoms. This is due to the cerebral adaptation occurring in hypernatremia. These include a gradual loss of intracellular osmolytes, lowering the osmotic gradient between the blood and the brain[96]. When serum sodium falls over 24 – 48 hours, it overwhelms the above compensatory mechanisms. This leads to severe cerebral edema and symptoms[6,97].

The physical findings are dependent on the degree and the chronicity of hyponatremia. Most abnormal findings on physical examination are neurological in origin[94,98,99].

Patients with hyponatremia may have symptoms of an underlying disease. Various studies[9,100,101] has shown association of hyponatremia with pulmonary and central nervous system diseases. So, the clinician should have suspicion of hyponatremia in patients with respiratory symptoms suggestive of pneumonia, pulmonary tuberculosis, pulmonary abscess, bronchiectasis, malignancies and chronic obstructive pulmonary disease. Patients with symptoms suggestive of central nervous system infections, trauma, vascular accidents or tumors should be evaluated[12]. Hyponatremia may complicate the clinical course of many acute neurologic and neurosurgical disorders[84].

Evidence for malignancy should be looked for in every patient. Hyponatremia associated with malignancies may be secondary to ectopic anti-diuretic hormone secretion or chemotherapy or undercurrent infections.

Many drugs alter the sodium metabolism. Individuals who are on these medications have preponderance to develop hyponatremia[54]. History related to drug intake is essential. Drugs such as amiodarone, lisinopril, digoxin, chlorpropamide, tolbutamide, desmopressin, clofibrate, clozapine, theophiline, carbamazepine, opiates, oxytocin, thiazides, prostaglandin synthesis inhibitors, nicotine, phenothiazines, selective serotonin re-uptake inhibitors, antipsychotics, tricyclic antidepressants, trazodone, vincristine, cyclophophomide and NSAID's[1] are known to cause hyponatremia[35].

Patients with history of persistent vomiting and diarrhea, on inadequate parenteral nutrition and reduced dietary intake can develop hyponatremia. These

patients are usually dehydrated or volume depleted and they tend to develop hypovolumic hyponatremia. Clinically these patients present with features of hypovolumia like dry mucous membranes, sunken eyes, tachycardia or orthostatic hypotension[12]. A study done by Kende M et al over a period of two years at Port Moresby General Hospital observed that hyponatremia was higher among patients with diarrhea and vomiting[11]. Lee et al noticed that all commonest cause for hyponatremia was gastrointestinal diseases.

Hyponatremia should also be suspected in patients with symptoms of congestive cardiac failure[77,78], renal failure and cirrhosis. Even mild hyponatremia was significantly associated with the higher mortality of patients with stable CHF. Persistent hyponatremia have a higher risk of events in patients with heart failure than normonatremic patients despite similar clinical improvements. Patients with above mentioned clinical diseases are mostly on diuretic therapy and so, are at increased risk of developing hyponatremia. These patients are usually over-loaded with fluids and will have clinical features suggestive of fluid excess, such as pulmonary basal crepitations, S3 gallop, peripheral edema or ascites.

Patients with hyponatremia, who lack findings of hypovolumia or hypervolumia, are considered to have euvolumic hyponatremia. Euvolumic hyponatremia is seen in patients with etiologies like exogenous free water load, hypothyroidism[70,71] cortisol deficiency[73], hypo-pituitarism[72] or SIADH[9].

Patients with viral, bacterial, protozoal, mycoplasmal, fungal infections are predisposed to hyponatremia. So an index of suspicion for hyponatremia is essential in patients with these infections. Hyponatremia occurs commonly in patients with AIDS and is associated with higher morbidity and mortality in these patients.

Among hospital in-patients use of hypotonic fluids and in post-operative patients are at risk for hyponatremia mostly due to improper fluid management or irrigating fluids[64,65].

Psychiatric patients are prone to develop hyponatremia either due to medications or to polydipsia[74,75]. Hyponatremia can also exacerbate psychiatric symptoms.[35] Persons with substance abuse as MDMA (3,4 methylenedioxymethamphetamine)[10], diamorphine can develop hyponatremia. Hyponatremia is reported in marathon runners and athletes due to loss of solutes. Hyponatremia is known to occur among alcoholics.

Rhabdomyolysis is an occasional consequence of hyponatremia and should be considered in patients with muscle pain or tenderness. Seasonal variation was noted with the occurrence of hyponatremia. This was probably due to variations in the ambient temperature influencing insensible fluid losses that could possibly have altered hydration status and sodium balance.

The prognosis of hyponatremia is usually proportional to the severity of their co-morbid conditions. However, it is difficult to ascertain if the electrolyte

disturbances is the primary cause of the increased morbidity, or whether it is due to the underlying conditions.

The severity of symptoms and signs are generally more prominent in elderly patients due to their failure of homeostatic mechanisms. It can also be explained by the increase in use of sodium lowering drugs in the elderly such as selective serotonin reuptake inhibitors for depression, or thaizide diuretics for hypertension and secondary prevention of stroke.

Rapid recognition and optimal treatment of depressed serum sodium can reduce the risk of death and symptom severity, permit less intensive care, reduce the duration of hospitalization and associated costs, increase success in treatment of underlying co-morbid conditions, and improve quality of life[35].

DIAGNOSTIC APPROACH TO HYPONATREMIA

Serum osmolality

The initial approach to a hyponatremia patient is to measure the serum osmolality to determine if the hyponatremia represents a true hypo-osmolar state. Thus, in a patient with hyponatremia, normal or elevated effective serum osmolality suggests the presence of either pseudohyponatremia or increased concentration of other osmoles, such as glucose and mannitol[62].

In the context of marked hyperlipidemia (hyper-triglyceridemia) and lactescent serum, lipids occupy a significant space in the volume of serum, leading to lower readings in the concentration of sodium and free water per litre

of serum. But physiologically the serum osmolality, the amount of water and concentration of sodium in serum remain unaffected. Newer methods using ion-selective electrodes in the measurement of serum electrolytes may avoid this problem.

In the presence of osmotically active substances (e.g., hyperglycemia or mannitol infusions), an increase in serum osmolality is observed, which results in movement of water out of the cells and subsequently a reduction of the serum sodium level by dilution. It has been calculated that every increase of 3.4 m mol/L in the serum glucose level will draw enough water out of the cells to reduce the serum sodium concentration by 1 m mol/L. However, recent evidence suggests that the hyperglycemia induced decrease in sodium concentration is considerably higher than the "standard" correction factor of 1.6, especially when glucose levels are greater than22.2 m mol/L. Hillier and colleagues[63] have proposed that a correction factor of 2.4 m mol/L is a better overall estimate of the association between sodium and glucose levels.

Urine osmolality

If a hypo-osmolar state is confirmed, the next step is to determine whether the ability of the kidney to dilute the urine is intact by measuring urine osmolality[158]. The normal response of the kidney is to excrete maximally dilute urine. If urine is maximally dilute, it indicates that anti-diuretic hormone (ADH) secretion is completely and appropriately suppressed, a finding seen in patients

with primary polydipsia or reset osmostat syndrome[62]. Hyponatremia is unlikely to develop in the setting of an intact urine diluting mechanism. However, Gillium et al reported patients who ingest large amounts of water, in isolated instances of more than 10 to 15 liters per day can develop hyponatremia. In these cases, a tendency to hyponatremia will be unmasked and enhanced by a concurrent impairment in water excretion. This can occur in the setting of central nervous system dysfunction and in antipsychotic agents, or it may be due to nausea or stress induced ADH secretion. Another unusual situation, in which modest amounts of fluid intake can lead to hyponatremia even when the urine diluting ability is intact, is observed in cases of extremely reduced solute intake. In these patients, the ability to excrete water is reduced by a poor dietary intake of salt. This phenomenon has been described in patients with chronic alcoholism and is often referred to as “beer potomania syndrome”.

Urine sodium concentration

In patients with hyponatremia, it is particularly important to assess the effective arterial blood volume. A decreased in blood volume is by far the most common cause of hyponatremia in clinical practice.

Hypovolumia can be determined clinically, by the presence of postural changes in blood pressure and pulse rate. Measurement of volume and

electrolyte level in urine is extremely useful in the assessment of effective arterial blood volume. Patients with volume depletion exhibit low urinary excretion of sodium and chloride (sodium level less than 20 m mol/L., chloride levels less than 20 m mol/L). An urine sodium level of less than 20 m mol/L in hypovolumia is relevant if renal salt wasting does not exist. On the other hand, an increased urine sodium level, a level above 40 m mol/L is usually observed in patients with euvolumic hyponatremia. In individuals with low dietary intake of salt, the urine sodium concentration in euvolumic hyponatremia may be less than 20 m mol/L.

An increased urine sodium concentration, greater than 40 m mol/L, is also found in sodium wasting condition, such as recent diuretic therapy, certain renal parenchyrnal diseases, adrenal insufficiency and metabolic alkalosis. Hyponatremia is common with thiazide diuretics, which act on the distal convoluted tubule by interfering with dilution of urine.

The ability of the kidney to conserve sodium and dilute the urine is impaired in patients with progressive renal disease owing to associated osmotic diuresis. However, the capacity of water excretion is relatively maintained in mild to moderate renal disease. Water retention and hyponatremia are seen only when the glomerular filtration rate falls to very low levels. In patients with chronic renal failure, salt wasting seems to occur only after acute reductions in salt intake.

In metabolic alkalosis related to volume depletion, urinary chloride excretion is low, to less than 10 to 20 m mol/L, owing to increased renal reabsorption of chloride. So, determination of the urine chloride level may help and this index is sometimes preferred to the urine sodium level as a measure of extra cellular volume.

In patients with urine sodium levels between 20 to 40 m mol/L, the response of serum sodium and its fractional excretion ($FE\text{-}Na^{+}$) to the administration of normal saline (one to two liters per day for one to two days) can be used to establish a correct diagnosis. An increase of less than 5 m mol/L in serum sodium levels and an increase of greater than 0.5% in $FE\text{-}Na^{+}$ is highly suggestive of SIADH, whereas an increase in serum sodium levels greater than 5 m mol/L and an increase of less than 0.5% in $FE\text{-}Na^{+}$ is evident in patients with hypovolemia.

Evaluation of causes of the syndrome of inappropriate diuretic hormone secretion

Patients with hyponatremia due to SIADH may require radiological and sonological assessment to rule out pulmonary, central nervous system and gastrointestinal diseases or disorders.

Hormonal disorders

It is of interest that the sodium concentration may be low, as much as 130 m mol/L, in pregnant women. This is due to human chorionic-gonadotropin hormone induced release of relaxin. Relaxin is associated with a downward resetting of serum osmolality.

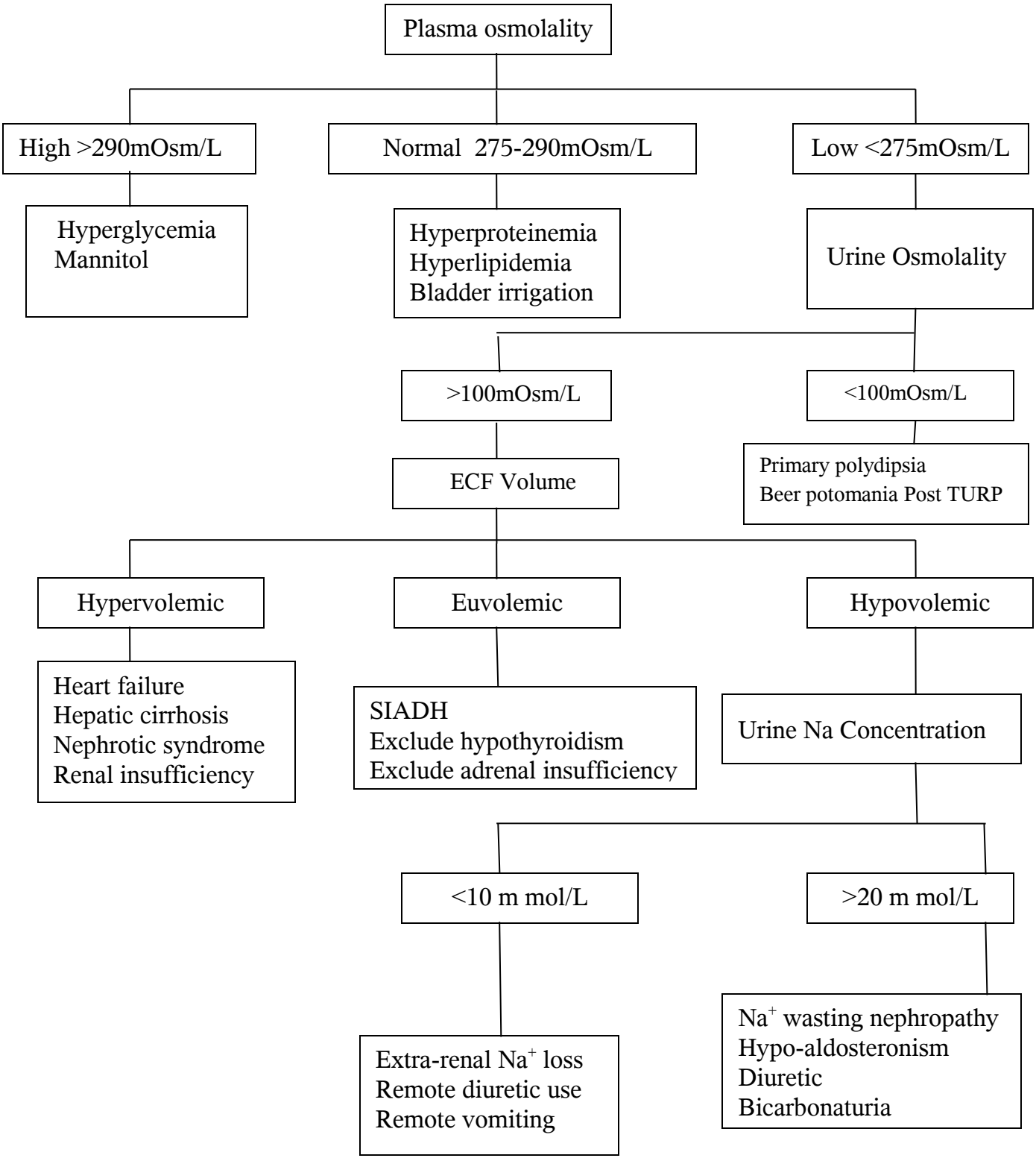
Hyponatremia can occur in the setting of primary or secondary adrenal insufficiency and hypothyroidism. Therefore, serum levels of thyroid stimulating hormone and random cortisol should be determined in cases of hyponatremia before a diagnosis of SIADH is made. Gluco-corticoid deficiency increases water permeability in the collecting tubules. Elevated ADH levels have been found in patients with gluco-corticoid deficiency. In patients with hypothyroidism, both ADH-mediated and intra-renal mechanism have been implicated in the pathogenesis of hyponatremia.

Acid-base status and potassium homeostasis

Acid-base status and potassium balance should be evaluated in certain cases of hyponatremia. For example, the presence of metabolic acidosis and hyperkalemia is suggestive of renal functional impairment or adrenal insufficiency, whereas a diarrhoeal syndrome is usually associated with metabolic acidosis and hypokalemia. Excessive vomiting or the use of diuretics may result in hyponatremia in association with metabolic alkalosis and hypokalemia. However, acid base status and potassium balance are not disturbed in SIADH. Additional electrolyte abnormalities which include

hypophosphatemia, hypokalemia and hypomagnesemia are frequently seen in hyponatremic patients, independently of hyponatremia cause.

ALGORITHM TO DIAGNOSE HYPONATREMIA



MATERIALS AND METHODS

Study area

Madras Medical College and Government General Hospital is one of the largest hospitals in South India located in Chennai Metropolis, Tamil Nadu catering the needs of over one crore people.

The Laboratory

The Biochemistry lab is a standardized laboratory. The methods used for estimation are:

Methods →

1. Serum Sodium – HILITE/Transaminase
2. Serum Potassium – I.S.ELECTRODE (Ion selective Electrophoresis)
3. UREA – Glutaraldehyde LDH
4. Creatinine – Jaffe Kinetic
5. SUGAR – (GOD/POD/Glucose oxidase peroxidase)
6. LFT – Enzymes – kinetic
7. TFT – Automated ELISA reader
8. Urine Na – I.S.ELECTRODE
9. Urine K – I.S.ELECTRODE
10. Lipids – ENZYMATIC METHOD
11. Urine osmolality – FREEZING POINT METHOD

Study Population

Patients admitted in Government General Hospital medical wards with serum sodium less than 130 mmol/L.

Type and duration of study

Cross section study, period of one and a half year (January 2008 to June 2009).

Inclusion Criteria

All inpatients >12 years of age with atleast two serum sodium values <130 mmol/L.

Exclusion Criteria

Patients with age less than 12 years and patients who are treated with Mannitol and osmotic diuretics.

Sample size and Technique

One hundred patients of Government General Hospital,Chennai.

The lab values of serum sodium of all patients from January 2008 to June 2009 was studied from which incidence of hyponatremia was calculated.

Out of this hyponatremic patients, a sample size of 100 patients were randomly selected by SIMPLE RANDOM SAMPLING, FROM THE TABLE OF RANDOM NUMBERS satisfying the inclusion criteria.

Data collection technique

In the hospital, all the patients', as routine, blood samples were taken and serum electrolytes were done in central biochemistry laboratory. The records were followed up for patients with hyponatremia and values repeated once for confirmation.

A standard proforma was used to record to detailed history of present complaints, past history including diabetes mellitus, systemic hypertension, Ischemic heart disease, dyslipidemia, neurological, chronic kidney disease / renal disease, regulatory and endocrine problems. A detailed drug history was also recorded.

Findings on clinical exam including volume status of patients were recorded.

Based on investigations and management of a patient, the following data was recorded.

Initial serum, sodium, final sodium at discharge/death, calculated serum osmolality, urine osmolality, urine spot sodium and endocrine work up (as and when required) were done.

The fluid management and drugs, if used were also noted.

The probable cause was correlated and the outcome of hospitalization was recorded.

STATISTICAL ANALYSIS

DESCRIPTIVE STATISTICS

The descriptive statistics – mean, median, standard deviation, minimum value, maximum value, range was used to describe the data.

1. Central tendency (Average)
    a. Arithmetic Mean (X)
    b. Median
    c. Mode
2. Measures of dispersion
    a. Range
    b. Standard deviation

The mean and standard deviation are calculated. The values between (a) 1 standard deviation on either side of mean will include 68% of values (b) values of twice the standard deviation from the mean will have 95% of values .These are “Confidence limits” of mean.

The data was entered into excel work sheet and above calculated.

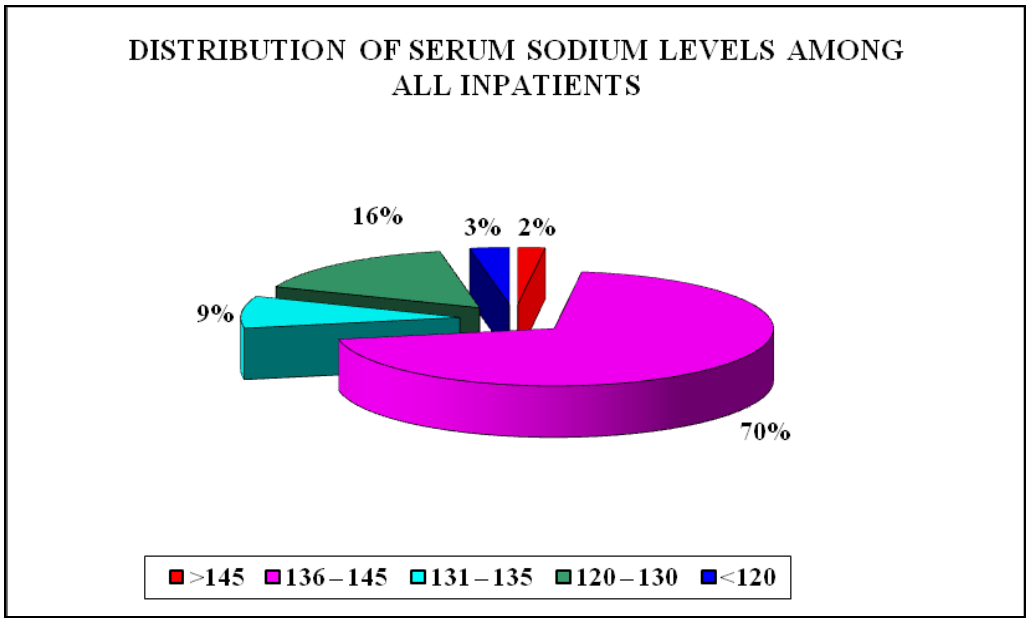
OBSERVATION AND RESULTS

The total number of hospital admission in medical wards was 25,326 and serum sodium estimates was done for 21,020 patients. The number of patients with hyponatremia less than 130 mmol/L was about 3980 patients (18.9%). The number of patients with severe hyponatremia with serum sodium less than 120 mmol/L was 620 patients (2.95%).

Distribution of serum sodium levels among all inpatients (21,020)

TABLE 4

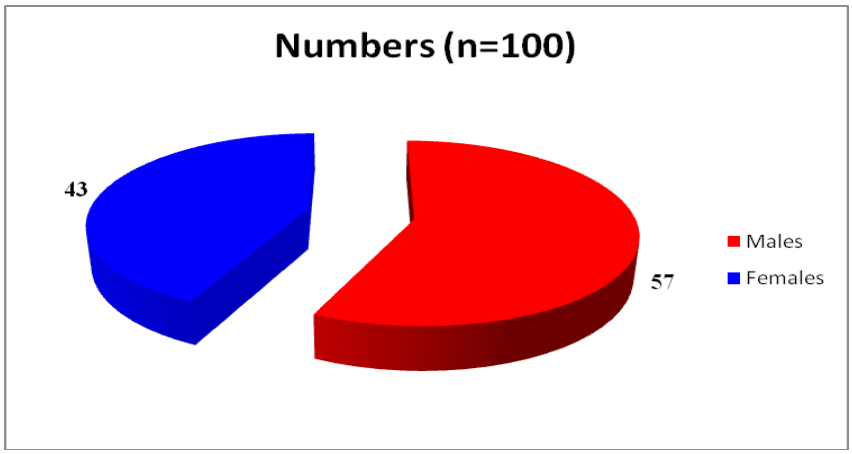
Range	No. of patients
>145	420
136 – 145	14714
131 – 135	1892
120 – 130	3384
<120	610
Total	21020



Out of the 21,020, 100 patients were selected. The observations arrived out of the 100 patients were as follows:

TABLE 5

	Numbers (n=100)
Males	**57**
Females	**43**

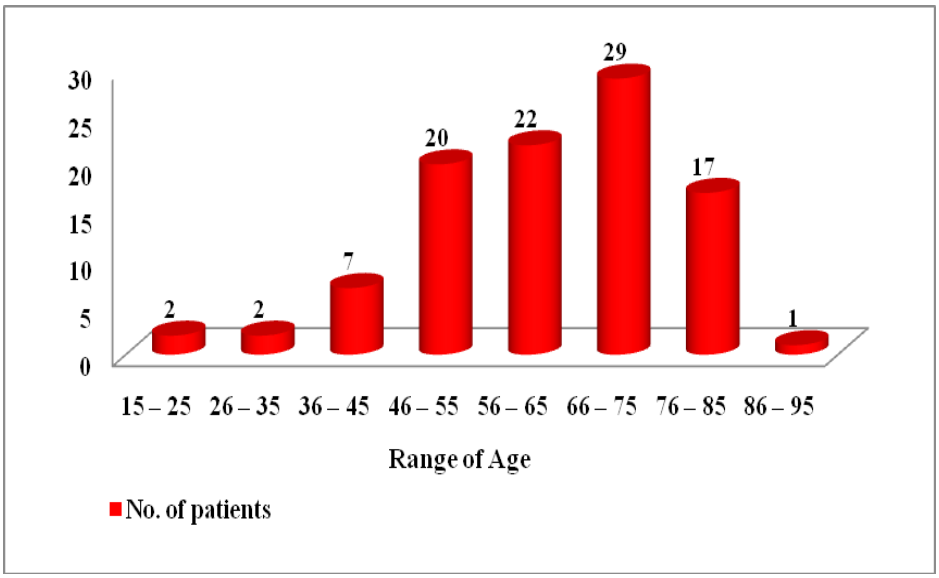


Age

Mean age of patients admitted was 62.46 years. Youngest age was 18 years old. The oldest age was 88 years.

TABLE 6

Range	No. of patients
15 – 25	2
26 – 35	2
36 – 45	7
46 – 55	20
56 – 65	22
66 – 75	29
76 – 85	17
86 – 95	1
Total	100



Hyponatremia development at admission/emergency ward/wards/ IMCU

92 patients had hyponatremia in wards.

Mode of admission

93% of patients prevented to emergency room with hyponatremia.

Admission to Intensive Care Unit

36% of patients were also admitted in IMCU and found to have hyponatremia.

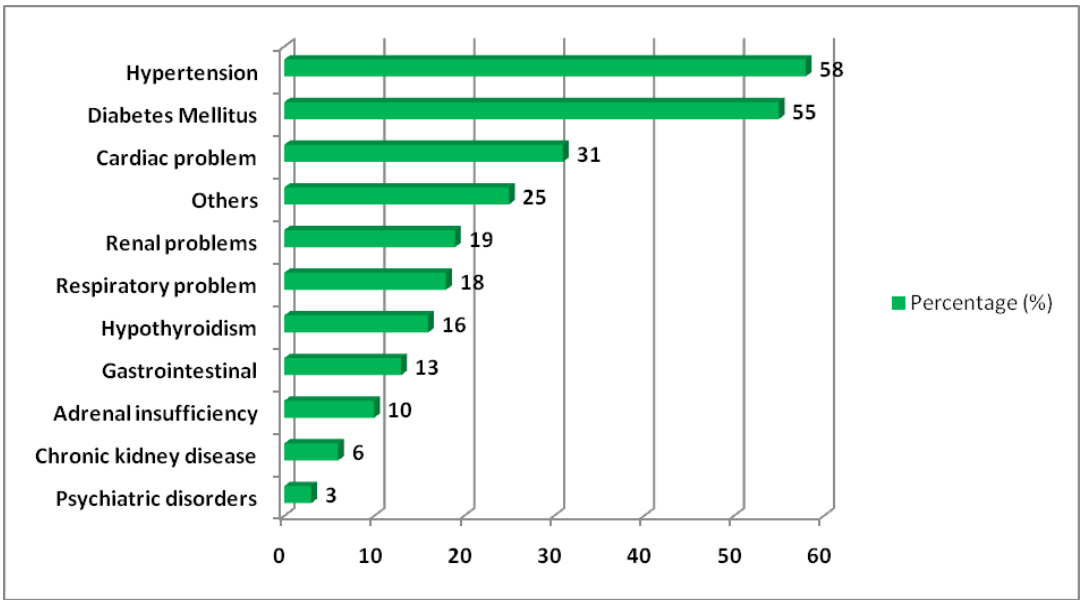
Co-morbid conditions

There were common chronic diseases with three patients like hypertension and diabetes mellitus.

Associated Chronic Diseases

TABLE 7

Disease	Percentage (%)
Psychiatric disorders	3
Chronic kidney disease	6
Adrenal insufficiency	10
Gastrointestinal	13
Hypothyroidism	16
Respiratory problem	18
Renal problems	19
Others	25
Cardiac problem	31
Diabetes Mellitus	55
Hypertension	58

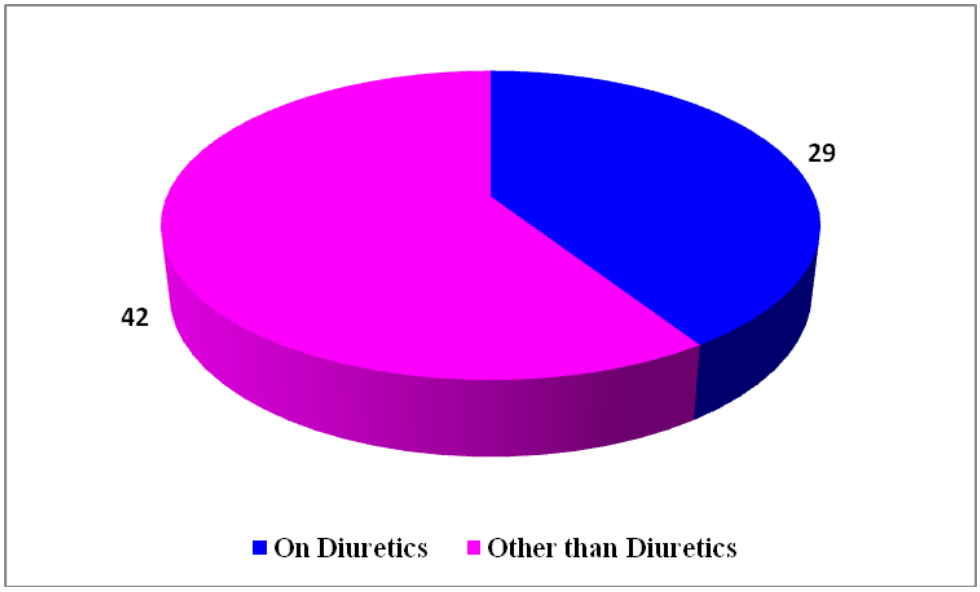


Drugs causing hyponatremia

29% of patients were on diuretics and 42% of patients were on drugs other than diuretics which causes hyponatremia.

TABLE 8

	Percentage (%)
On Diuretics	**29**
Other than Diuretics	**42**



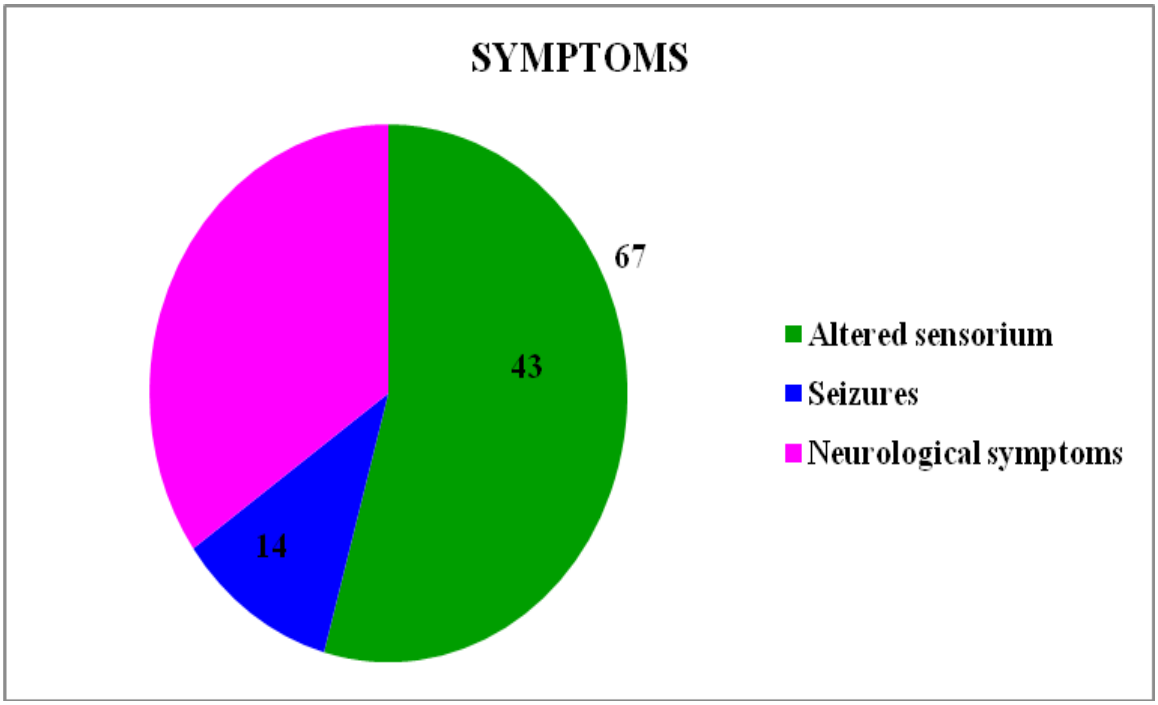
Symptoms

67 patients had some neurological symptoms of hyponatremia due to cerebral edema like nausea, vomiting, giddiness and altered sensorium. 14 patients presented with seizures.

The lower the sodium value, the higher the incidence of lymptamatic hyponatremia.

TABLE 9

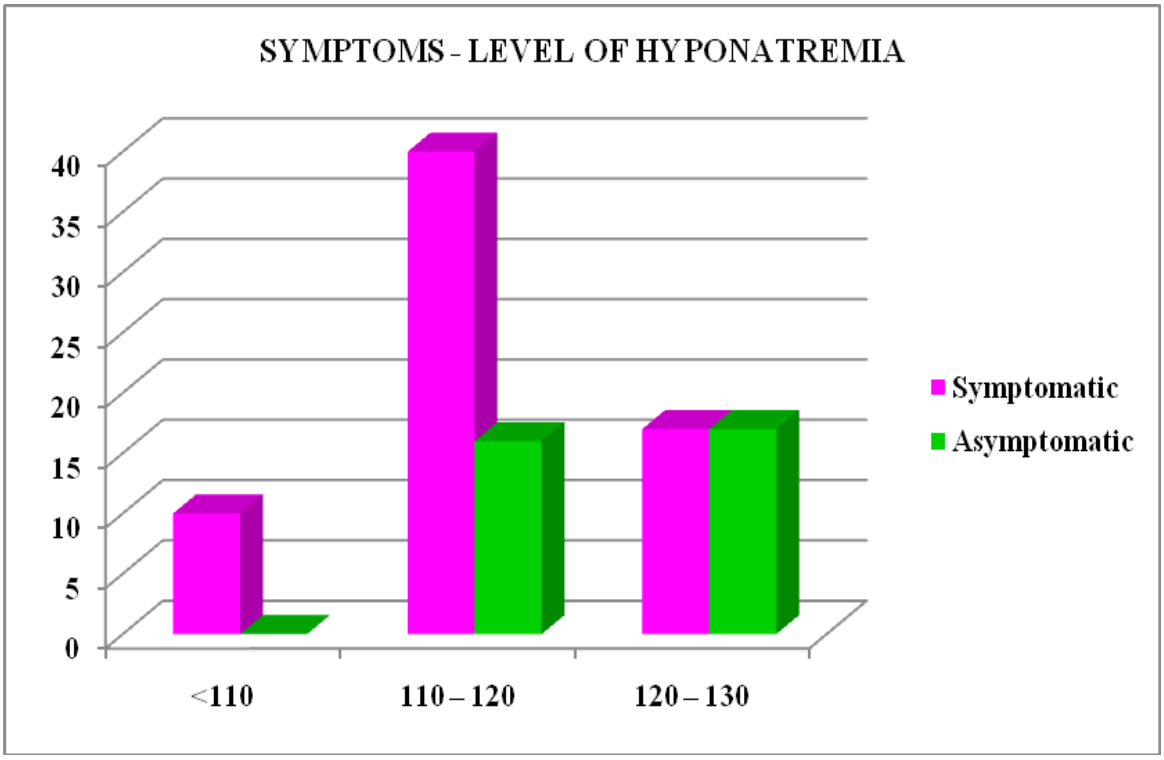
Symptoms	No. of patients
Neurological symptoms (Nausea, vomiting, giddiness, etc.,)	67
Altered Sensorium	43
Seizures	14



Symptoms – level of hyponatremia

TABLE 10

Range (n=10)	Symptomatic	Asymptomatic	P value
<110	10	0	<0.001
110 – 120	40 (71%)	16	<0.05
120 – 130	17 (50%)	17	0.32



The incidence of symptomatic hyponatremia is more with lowering sodium levels which is statistically significant. All patients with severe hyponatremia had symptoms.

VOLUME STATUS

TABLE 11

Volemic status	No. of patients
Hypervolemic	19
Hypovolemic	19
Euvolemic	62

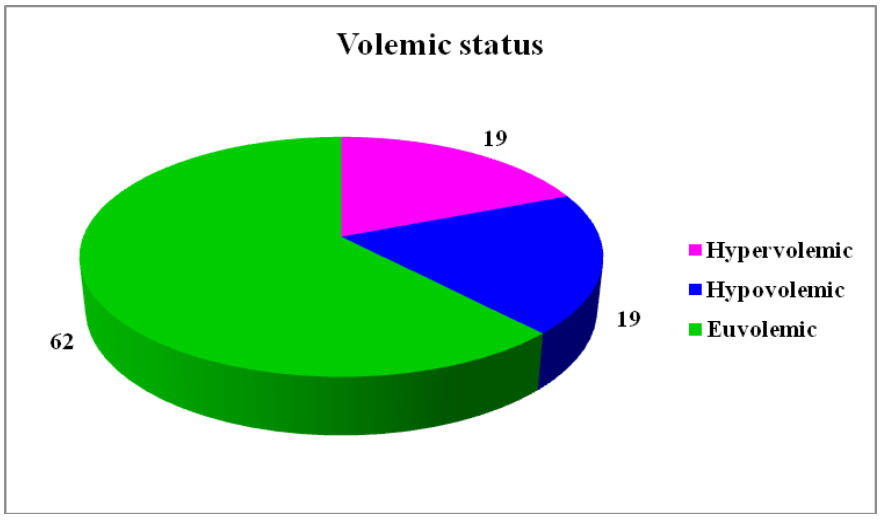
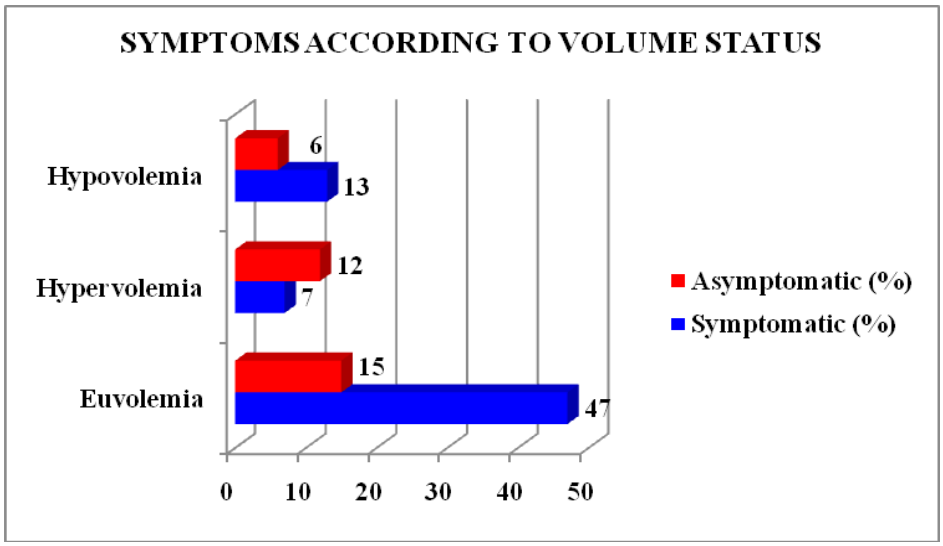


TABLE 12

SYMPTOMS ACCORDING TO VOLUME STATUS

Volume Status (n = 100)	Symptomatic (%)	Asymptomatic (%)	P value
Euvolemia	47	15	P<0.05
Hypervolemia	7	12	P = 0.46
Hypovolemia	13	6	P = 0.21



Most of Euvolemic patients were symptomatic (P<0.05). Most of the Hypervolemic patients were asymptomatic and most of Hypovolemic patients were symptomatic.

Initial sodium

The mean initial sodium was 118.6mEq/L with standard deviation of 5.4864.

Final sodium

The mean final sodium was 122.53mEq/L with standard deviation of 3.8755.

Laboratory investigations

All the 100 patients had calculated serum osmolality done. 92 patients had urine osmlality done. 78 patients had thyroid function tests done. 53 patients had serum cortirol / ACTH stimulation tests done.

16 patients had hypothyroid problems. 10 patients had adrenal insufficiency. (by ACTH stimulation test (Adreno Cortico Typical Hormone).

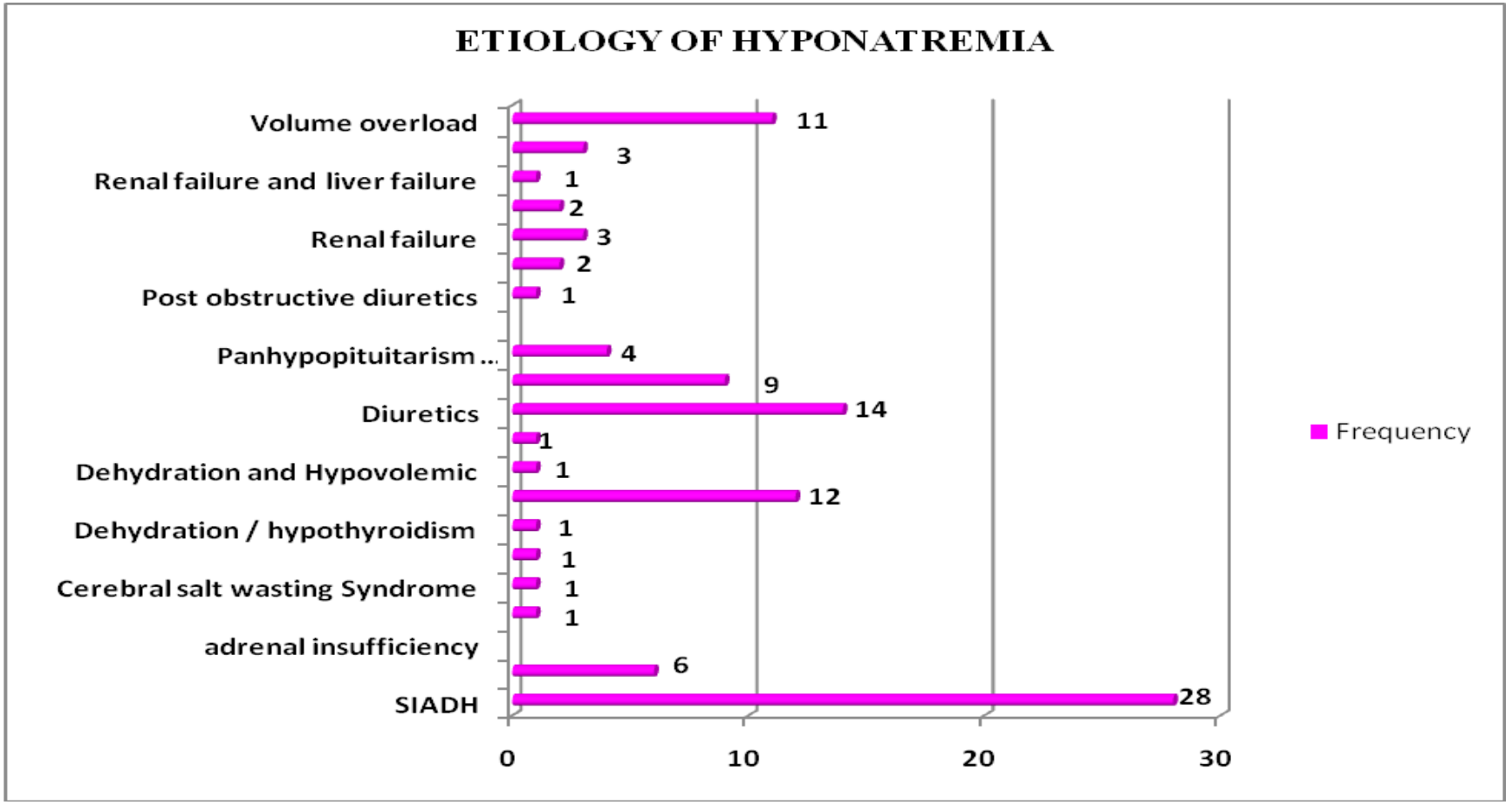
Primary diagnosis

The primary diagnosis as per discharge/death summary is tabulated as appendix. The most common diagnosis was metabolic encephalopathy followed by cardiac failure. Many patients has various infections.

TABLE 13

ETIOLOGY OF HYPONATREMIA

Cause of hyponatremia	Frequency
SIADH	28
Addison's disease / adrenal insufficiency	6
Adrenal pituitary	1
Cerebral salt wasting Syndrome	1
Dehydration / adrenal insufficiency	1
Dehydration / hypothyroidism	1
Dehydration / hypovolemic	12
Dehydration and Hypovolemic	1
Dilutional hyponatremia	1
Diuretics	14
Hypothyroidism alone	9
Panhypopitutarism (Hypothyroid + adrenal insufficiency)	4
Post obstructive diuretics	1
Pseudohyponatremia	2
Renal failure	3
Renal failure and ascites (volume overload)	2
Renal failure and liver failure	1
Unclear cases	3
Volume overload	11


ETIOLOGY OF HYPONATREMIA
Volume overload
Renal failure and liver failure
Renal failure
Post obstructive diuretics
Panhypopituitarism ...
Diuretics
Dehydration and Hypovolemic
Dehydration / hypothyroidism
Cerebral salt wasting Syndrome
adrenal insufficiency
SIADH
11
3
1
2
3
2
1
4
9
14
1
1
12
1
1
1
1
6
28
0
10
20
30
Frequency

The commonest cause of hyponatremia was SIADH. A lot of patients had endocrine causes. Hypothyroidism, Addison's and pituitary insufficiency.

TABLE 14

TREATMENT

Type of Treatment	Frequency
Normal Saline + Diuretics	43
Insulin, NS	1
NS+3% saline	5
Fluid restriction diuretics	4
Fluid restriction alone	1
3% saline	31
3% saline + diuretics	1
Dialysis	1
Steroids + NS	6
Diuretics	12

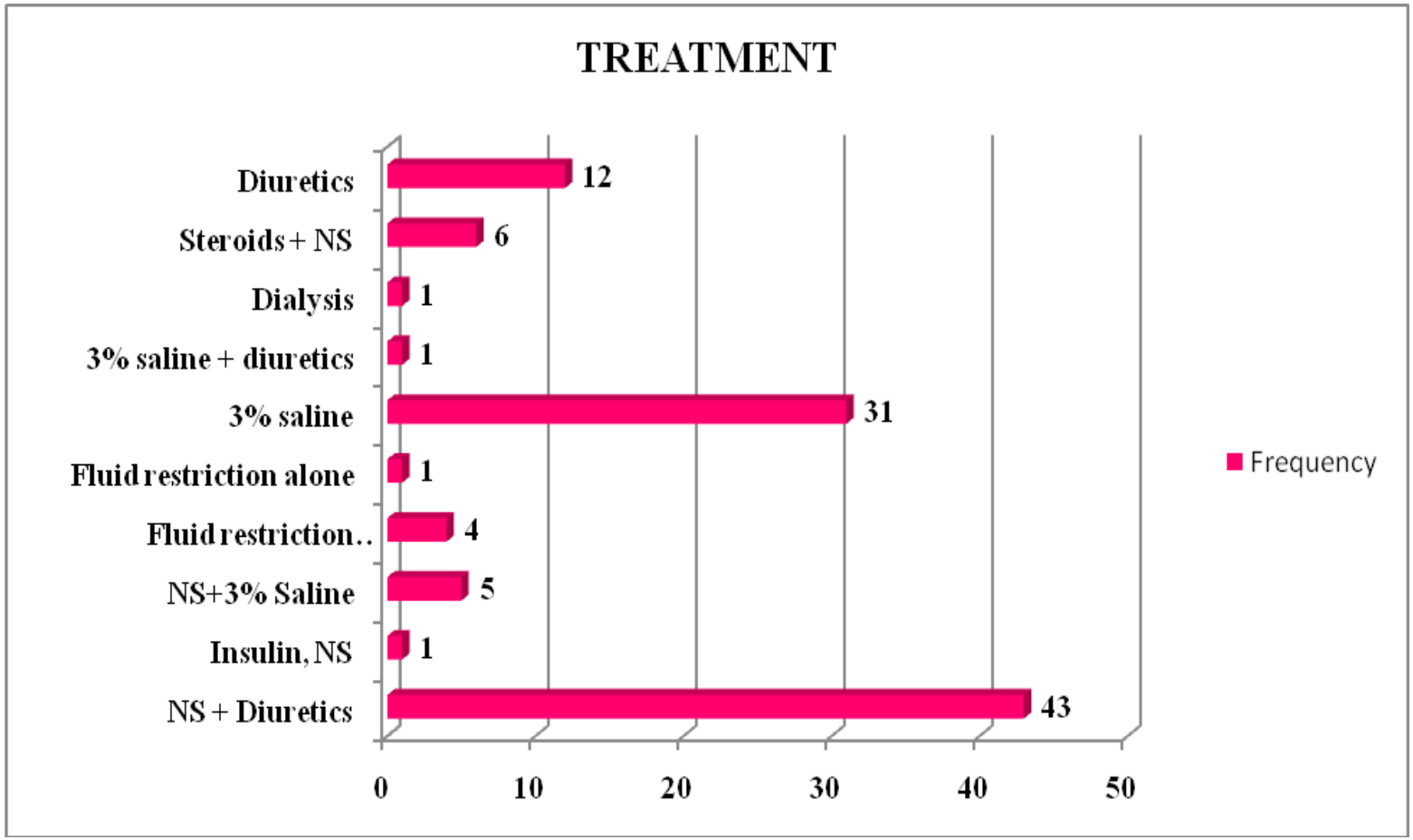
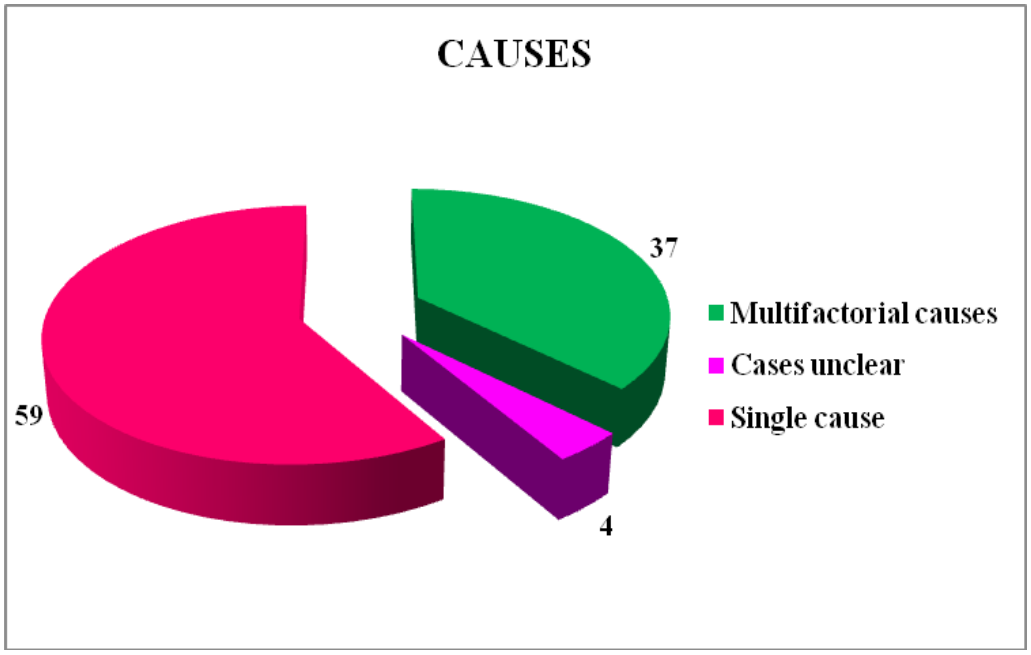

TREATMENT
Diuretics
Steroids + NS
Dialysis
3% saline + diuretics
3% saline
Fluid restriction alone
Fluid restriction..
NS+3% Saline
Insulin, NS
NS + Diuretics
12
6
1
1
31
1
4
5
1
43
0
10
20
30
40
50
Frequency

TABLE 15

CAUSES

	No.of cases
Multifactorial causes	37
Cases unclear	4
Single cause	59



Ninety patients improved, but of which one went into extrapontine myelinolysis but recovered.

Eight patients died

Two patients deteriorated / discharged against medical advise

TABLE 16

OUTCOME

	No.of cases
Improved	90
Died	8
Deteriorated / Against Medical Advise	2

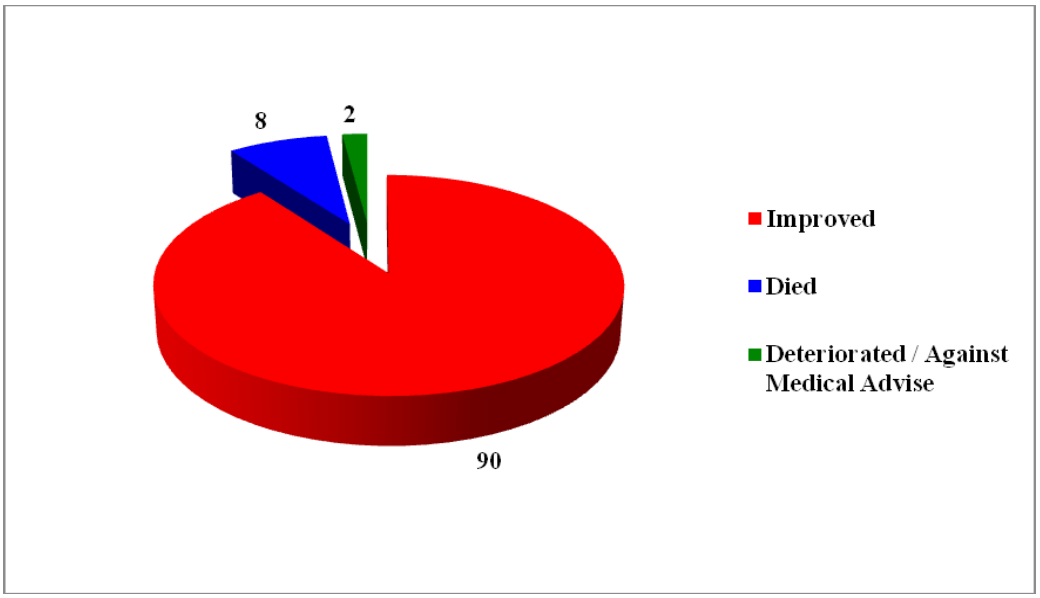


TABLE 17

Charecteristics of patients who died / deteriorated

	No. of cases
Males	4
Females	6

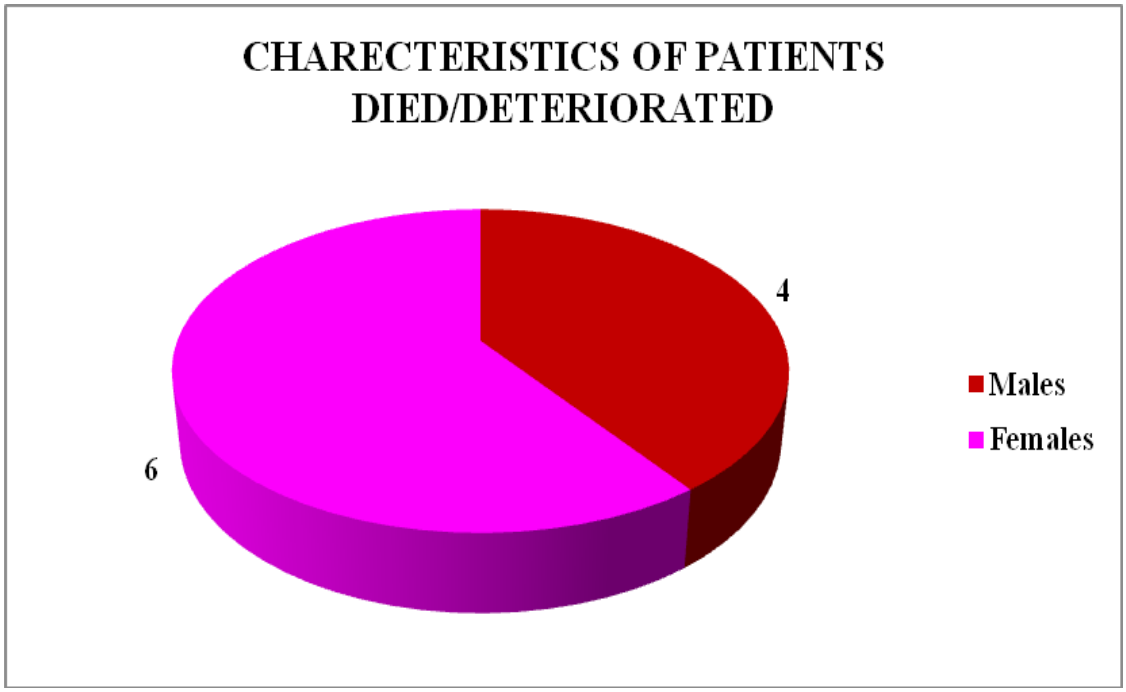
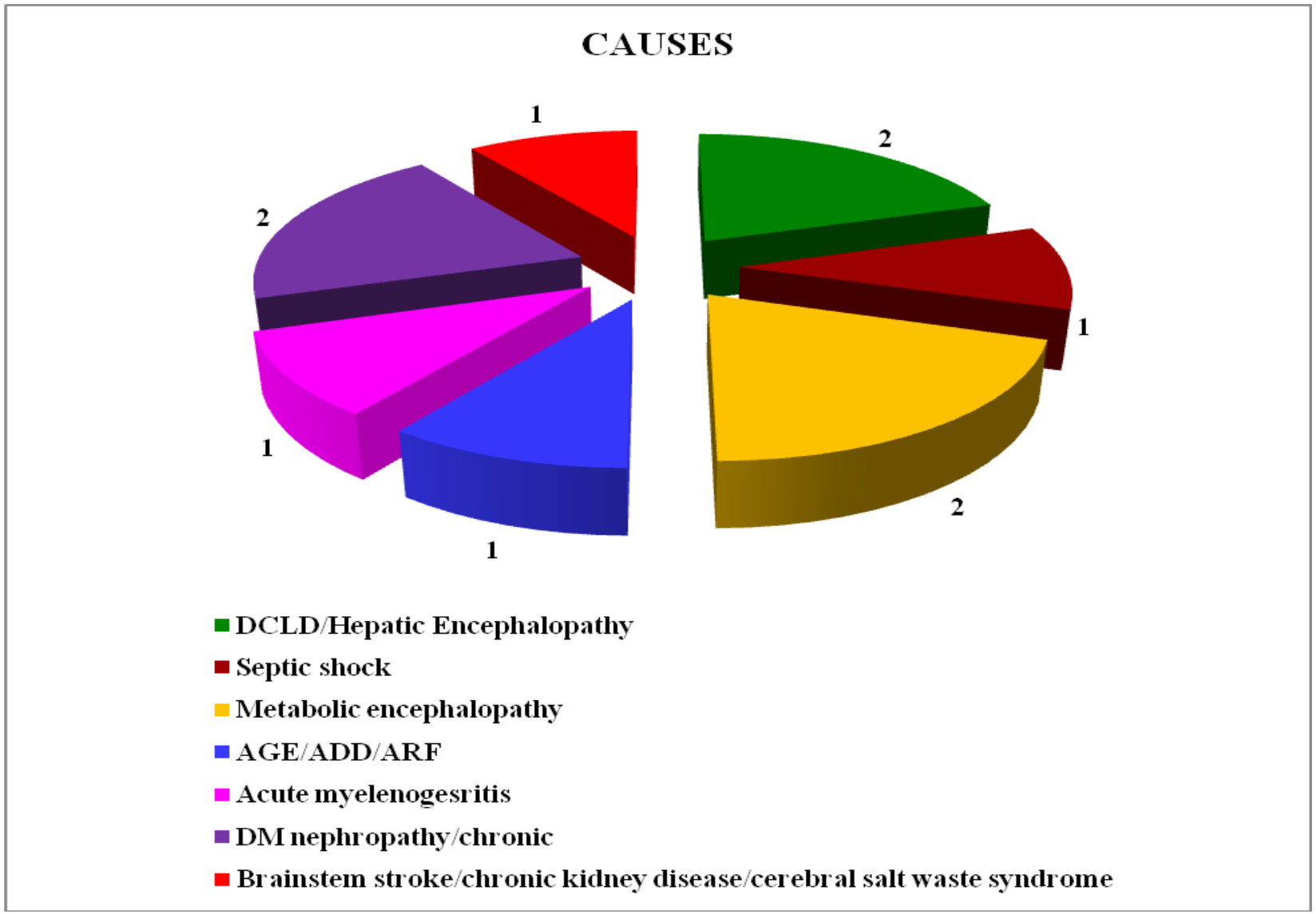


TABLE 18

CAUSES

Causes	No. of cases
DCLD/Hepatic Encephalopathy	2
Septic shock	1
Metabolic encephalopathy	2
AGE/ADD/ARF	1
Acute pyelonephritis	1
DM nephropathy/chronic	2
Brainstem stroke/chronic kidney disease/cerebral salt wasting syndrome	1


CAUSES
1
2
2
1
1
2
DCLD/Hepatic Encephalopathy
Septic shock
Metabolic encephalopathy
AGE/ADD/ARF
Acute myelenogesritis
DM nephropathy/chronic
Brainstem stroke/chronic kidney disease/cerebral salt waste syndrome

A report on mean initial and final sodium values are as follows:

Outcome	Initial sodium	Final sodium
Alive (N = 90)		
Mean	**118.628**	**122.64**
Standard Deviation	**5.090**	**3.8198**
Median	**119.5**	**124**
Maximum	**129**	**135**
Minimum	**106**	**114**
Died / deteriorated (N = 10)		
Mean	**115.8**	**121.2**
Standard Deviation	**3.8529**	**3.084**
Median	**116**	**120.5**
Maximum	**120**	**126**
Minimum	**108**	**116**
Total N = 100		

Total:	Mean	118.03	122.5
	Standard Deviation	8.020	3.768
	Median	119	123
	Maximum	129	135
	Minimum	106	114

The mortality did not correlate with severity of hyponatremia (p.value 0.125). The mortality depended on the underlying illness rather than severity of hyponatremia.

PRIMARY DIAGNOSIS OF PATIENTS

S.No.	Primary Diagnosis	No. of patients
1.	Bronchopneumonia/Acute bronchitis	6
2.	DM Nephropathy/LVF	2
3.	Brainstem stroke	3
4.	GBS/AIDP	2
5.	Diabetes Mellitus/Hyperglycemia	2
6.	AGE/ADD	4
7.	CKD	4
8.	Sepsis, Acute Renal Failure other than CKD	4
9.	DCLD/Hepatic Encephalopathy	3
10.	Addison's disease/Adrenal insufficiency	2
11.	Cardiac failure	10
12.	Metabolic encepholapathy	27
13.	Pericardial effusion	1
14.	Acute Infective cases	7
15.	Acute Coronary Syndrome	1
16.	Heat stroke	2
17.	Chronic diarrhea	2
18.	Fracture C6, C7 spine	1

S.No.	Primary Diagnosis	No. of patients
19.	Hypoadrenalism	1
20.	Seizure disorder	2
21.	Chronic SDH	1
22.	Post renal obstruction	1
23.	TB Meningitis	3
24.	Liver abscess	1

25.	**Hypopitutarism**	**3**
26.	**Post-operative**	**2**
27.	**Pulmonary TB**	**1**
28.	**Miliary TB**	**2**
29.	**Viral fever**	**4**
30.	**Ca Esophagus**	**1**
	N = 100 patients	**105** **(5 mixed causes)**

DISCUSSION

In the present study, the incidence of hyponatremia was (18.9%). The incidence was 6.9% in the study done by Hochman[103]. It was the most commonly ordered investigation among inpatients. During the period of the present study serum sodium was done in 8.2% of admitted patients.

The present study included patients with serum sodium less than 130 mEq/L. There were 57 males and 43 females with ratio of 1.32:1. In general, in our hospital population, there were more males than females. Hence, this slight increase in males was not very significant. This ratio was more or less constant in all age groups. But in the age group above 70 years both genders were equal and in the age group of above 80 years comprised of only females. No conclusion was made on this difference in incidence.

In the present study, hyponatremia was seen more commonly in patients above 45 years than in younger patients. The ratio between numbers of patients above 45 years in comparison of below 45 years 8.09:1. Similar trend was also observed by Hochman[103] Vurgese in their study has shown that elderly patients were more prone for hyponatremia. The mean age in the present study was 62.46 years which was comparable to studies by Anderson[9] where the mean age was 58 years and study done by Vuurgese[103] where the mean age was 57.05 $\pm$ 2SD.

The various factors responsible for hyponatremia in elderly are decreased glomerular filtration rate, impaired ability of kidney to conserve sodium, increased release of arginine vasopressin to a given osmotic stimulus, various drugs taken by them, decreasing appetite and concomitant illnesses.

Based on serum sodium concentration hyponatremia was classified as mild, moderate and severe with serum sodium 121 – 130mEq/L, 111 – 120mEq/L and less than or equal to 110mEq/L respectively. There were 10(10%) patients with mild hyponatremia. The degree of hyponatremia could more or less predict the symptoms of hyponatremia. Some patients with serum sodium greater than 120mEq/L had neurological symptoms like drowsiness. But patients with serum sodium less than or equal to 110mEq/L showed severe neurological symptoms like seizures and unconsciousness.

In study by Hochman[103] et al, there were 39% patients with mild hyponatremia and rest 61% had moderate to severe hyponatremia. The presence or absence of symptoms and severity was more related to rapidity of fall of serum sodium rather than the amount of fall. The elderly patients with chronic hyponatremia can tolerate lower levels of hyponatremia without any symptoms. Hence, we conclude the more severe the hyponatremia and rapid fall of sodium more severe the symptoms.

While analyzing history, 33% patients were only symptomatic and 67% were with neurological symptoms.

In the study done by Hochman[103], there were 43.4% patients with asymptomatic , 39.9% who had mild symptoms and 16.7% patients has severe neurological symptoms with stupor and coma. The mean serum sodium for asymptomatic patients was 120.26 and symptomatic was 116.88mEq/L. The percentages of patients and mean serum sodium in the two groups are summarized in the following table, in comparison with study by Hochman.

Table 19

	Hochman		Present study	
Symptoms	**% Patients**	**Mean serum**	**% Patients**	**Mean Serum Na**
Asymptomatic	43.4%	123	33%	120.26 $\pm$ 3.27
Symptomatic	86.6%	120.8	67%	116.88 $\pm$ 5.39

The percentage of patients in various groups in the present study varies markedly with the above study. The reason for this variation was probably due to the limited number of patients and selection criteria in the present study. The mean serum sodium was slightly lower in all the groups in the present study as compared to the previous study except in the asymptomatic group.

The hydration status of the patients was diagnosed on the basis of clinical examination and was divided into euvolumic, hypovolumic and hypervolumic states. In the present study 62 patients were euvolumic, 19 patients were

hypovolumic and 19 patients were hypervolumic representing 62%, 19% and 19% of the patients respectively.

Table 20

Hyponatremia	Hochman (%)	Anderson (%)	Present study (%)
Euvolumia	**50**	**34**	**62**
Hypovolumia	**30.5**	**35**	**19**
Hypervolumia	**19.5**	**31**	**19**

This correlated with other studies where euvolumic hyponatremia was the commonest. Further, SIADH was the most common diagnosis among this group of patients. In study by Anderson[9], 34% had euvolumia, 35% had hypovolumia and 31% had hypervolumia. In study by Hochman[103], 50% patients had euvolumia, 30.5% had hypovolumia and 19.5% had hypervolumia (Table 16).

Patients with euvolumia were more symptomatic and had more severe symptoms of hyponatremia compared to the other groups. The average serum sodium was 117mEq/L. 75.8% of these patients were symptomatic with neurological symptoms.

In the study done by Vurgese[104], the incidence of hyponatremia was 3.6% with the definition of hyponatremia as serum sodium levels ≤130m mol/L. The study population consisted of 66 patients with 56% males and 44% females. The mean age was 57.05 ± 2SD. The commonest age group affected was 45 to 64 years

(72.8%) and the least affected group was 12 to 25 years. The common cause for hyponatremia was SIADH and pneumonia was the commonest cause of SIADH leading to hyponatremia. One of the causes of SIADH was due to HIV infection. Renal failure and congestive cardiac failure was the next frequent causes of hyponatremia. A majority of the patients (82%) showed mild to moderate hyponatremia (120 – 130 m mol/L). Seasonal variation was noted in the study with 59.1% patients presenting in the summer months. The comparison of the present study with the study done by Vurgese[104] is given in Table .

Table 21

	Vurgese	**Present Study**
Incidence	**3,6%**	**18.9%**
Study population		
Male	**56%**	**57%**
Female	**44%**	**43%**
Mean age	**57.95 ± 2SD**	**62.46 ± 14.4**
>45 years with Hyponatremia	**722.8%**	**89%**
Common causes	**SIADH**	**SIADH**
Other causes	**Renal Failure, CCF**	**CCF, Renal Failaure**

On the whole, SIADH was the most common cause of hyponatremia in the present study representing 28% of cases. In other studies by Hochman[103], SIADH represented 28.3% of cases, 34% in the study by Anderson[9] and 34.8% in the study by Vurgese[104].

In patients with euvolumic hyponatremia, 26 patients satisfied the criteria to diagnose SIADH. They had low serum osmolality, high urine osmolality and high urine sodium. However, in 2 patients in whom there were no other illness or in whom cause of SIADH was not obvious, we did other investigations like thyroid function tests and serum cortisol. In patient in whom the cause of SIADH was obvious like stroke, we did not do thyroid function and serum cortisol.

The mean urine sodium was 66.29 $\pm$ 37.04 mEq/L and urine osmolality was 286.7 $\pm$ 135.09 m Osm/L. Urea and creatinine values were lower inpatients with SIADH. Mean urea was 23 mg% and creatinine was 0.95 mg%. Serum urea and creatinine are useful, as they generally are low and usually urea less than20 and creatinine less than 0.9 in most cases. This might indicate an underlying SIADH.

Thyroid function tests and adrenal function

Thyroid function tests and random serum cortisol/ACTH stimulation estimation test was done in a large number of patients. There were a relatively large number of patients with hypothyroidism (9%), adrenal insufficiency (6%) and panhypopituitarism (4%). Although these endocrine abnormalities are known to cause hyponatremia, occurrence of these abnormalities in a relatively large susbset of patients needs to be considered and endocrine work-up must be a part of investigations for severe hyponatremia.

16% of patients had hypothyroidism and 10% had hypoadrenalism. Patients with hypothyroidism and hypoadrenalism had presentation similar to SIADH. However, other features associated with these condition help to differentiate them from SIADH. Before the diagnosis of SIADH, the above diseases should be excluded by appropriate investigations.

Patients with hypovolumic hyponatremia also had predominant moderated hyponatremia. Among 7 patients with hypovolumic hyponatremia, one patient had cerebral salt wasting syndrome.

Majority of patients with hypervolumic hyponatremia had mild hyponatremia. The mean serum sodium was 116.7 mEq/L.

Treatment and monitoring

Monitoring of sodium was done on a 6 hourly to12 hourly basis in most of the patients with symptomatic and severe hyponatremia. Fluid correction depended on the type, cause and present of symptoms.

The mean rate of correction was adequate and comparable with most of the international studies. Normal saline alone, 3% saline, fluid restriction, + duration, dialysis, steroids alone and in combination were used to treat symptomatic and severe hyponatremia. One patient went into extra pontine myelinolysis but recovers with steroids and physiotherapy. The mortality in this study (death/deterioration and against medical advice) is around 10% which is relatively low compared to

other studies. The mortality depended on severity of the underlying illness rather than the initial serum sodium, final serum sodium or the rate of correction.

The incidence of hyponatremia (18.9%) in our study correlates well with most of the other studies and estimates the high incidence of hyponatremia medical wards. A number of studies have evaluated the incidence and etiology of hyponatremia in general, but there are very few relevant studies related to hyponatremia in inpatients in medical wards. Delineating the cause of hyponatremia is important in order to impart specific treatment tailored to the etiology.

CONCLUSIONS

1. Symptomatic hyponatremia is common among the hospitalized patients.
2. Neurological symptoms are common in hyponatremia patients
3. SIADH and euvolumic hyponatremia formed the largest subgroup in the study.
4. Drugs, especially diuretics, are a common cause of hyponatremia.
5. A relatively large number of patients had endocrine abnormalities (thyroid, adrenal and pituitary).
6. The mortality was about 10%. It was mainly due to underlying primary diseases.
7. Older age groups had more incidence of hyponatremia.
8. Symptoms of hyponatremia increased with severity of hyponatremia.

BIBLIOGRAPHY

1. Yeates KE, Singer M, Morton AR. Salt and Water: a simple approach to hyponatremia. *CMAJ* 2004; 170(3): 365 – 9.

2. Gone NE, Kandemire N, Sen Y, Yordam N, Hyponatremia can be a presenting finding of multiple pituitary hormone deficiency in children: report of a case and review of literature. *Clin Pediatr* 2005; 44: 623 – 628.

3. Bhananker SM, Paek R, Vavilala MS. Water intoxication and symptomatic hyponatremia after outpatient surgery. *Anesth Analg* 2004; 98: 1294 – 6.

4. Coenraad MJ, Meinders AE, Vandenbroucke JP, Frolich M, Taal JCW, Bolk JH. Causes of hyponatremia in the departments of internal medicine and neurosurgery. *European Journal of Internal Medicine* 2003; 14: 302 – 309.

5. Douglas I. Hyponatremia: Why it matters, how it presents, how we can manage it. *Cleveland Clinic Journal of Medicine* 2006; 73: S4 – S12.

6. Berl T. Treating hyponatremia; damned if we do and damned if we don't. *Kidney Int* 1990; 37(3): 1006 – 18.

7. Arinzon Z, Feldman J, Jarchowsky J, Fidelman Z, Krasnyansky I, Adunsky A. A comparative study of the syndrome of inappropriate antidiuretic hormone secretion in community-dwelling patients and nursing home residents. *Aging Clin Exp Res* 2003; 15: 6 – 11.

8. Janicic N, Verbalis JG. Evaluation and management of hypo-osmolality in hospitalized patients. *Endocrinol Metrab Clin North Am* 2003; 32: 459 – 481.

9. Anderson RJ, Chung HM, Kluge R, Schrier RW. Hyponatremia: a prospective analysis of its epidemiology and the pathogenetic role of vasopressin. *Ann Intern Med* 1985; 102: 164 – 168.

10. Hsu YJ, Chiu JS, Lu KC, Chau T, Lin SH. Biochemical and etiological characteristics of acute hyponatremia in the emergency department. *The Journal of Emergency Medicine* 2005; 29(4): 369 – 374.

11. Kende M, Ray U, Hanhupa B. Review of cases of hyponatremia in the Port Moresby General Hospital between August 1993 and June 1995. *Med J* 1999; 42(3-4): 84 – 9.

12. Diringer MN, Zazulia AR. Hyponatremia in neurologic patients: consequences and approaches to Treatment. *The Neurologist* 2006; 12: 117 – 126.

13. Miller M. Hyponatremia: age-related risk factors and therapy decisions. *Geriatrics* 1998; 53: 32 – 42.

14. Natkunam A, Shek CC, Swaminathan R. Hyponatremia in a hospital population. *J Med* 1991; 22(2): 83 – 96.

15. Fegan G, Begley J. Hyponatremia in the elderly. *CME Geriatr Med* 2005; 7: 76 – 85.

16. Kugaler JP, Hustead T. Hyponatremia and hypernatremia in the elderly. *Am Fam Physician* 2000; 61: 3623 – 30.

17. Schrier RW. Body fluid volume regulation in health and disease: a unifying hypothesis. *Ann Intern Med* 1990; 113: 155 – 159.

18. Young A. Ageing and physiological function. *Philos Trans R Soc Lond B Biol Sci* 1997; 352: 1837 – 1843.

19. Beck LH. The aging kidney: Defending a delicate balance of fluid and electrolytes. *Geriatrics* 2000; 55: 26 – 28.

20. Fulop T, Worum I, Csongor J, Foris G, Leovey A. Body composition in elderly people: Determination of body composition by multiisotope method and the elimination kinetics of these isotopes in healthy elderly subjects. *Gerontology* 1985; 31: 6 – 14.

21. Allison SP, Lobo DN. Fluid and electrolytes in the elderly. *Curr Opin Clin Nutr Metab Care* 2004; 7: 27 – 33.

22. Melvin C, Graeme EH, Soiza RL. Prognostic implications of hyponatremia in elderly hospitalized patients. *Archives of Gerontology and Geriatrics* 2007; 45: 253 – 258.

23. Scott MG, LeGrys VA, Klutts JS. Electrolytes and blood gases. Tietz textbook of clinical chemistry and molecular diagnostics 2006. Saunders WB. *Philadelphia. 3rd ed*: 983 – 1018.

24. Edelman IS, Liedman J. Anatomy of body water and electrolytes. *Am J Med* 1959; 27: 256.

25. Zinmermann EA. Anatomical basis of thirst and vasopressin secretion. *Kidney Int* 1987; 32: SI4.

26. Robertson GL. Thirst and vasopressin function in normal and disordered states of water metabolism. *J Lab Clin Med* 1983; 101:351 – 4.

27. Robertson GL. Osmo-regulation of thirst and vasopressin secretion in human subjects: Effect of various solutes. *J Hum Physio* 1983; 244: E607.

28. Anderson B. Thirst and its disorders. *Annu Rev Med* 1982; 3: 231 – 2.

29. Robertson GL. The osmo-regulation of vasopressin. *Kidney Int* 1976; 10: 25.

30. Schrier RW. Osmotic and non-osmotic control of vasopressin release. *Am J Physio* 1979; 236: F321.

31. Norsk P. Influence of low and high pressure baro-reflexes on vasopressisn release in human. *Act Endocrinol* 1989; 121: 3 – 4.

32. Rowe SK. Influence of emetic reflex on vasopressin release in man. *Kidney Int* 1979; 16: 729 – 30.

33. Baylis OPH, Thompson GJ. Osmoregulation of vasopressin and secretion and thirst in health and disease. *Clin Endocrinol* 1988; 29: 549 – 576.

34. Mc Kenna K, Thompson GJ. Osmoregulation in clinical disorders of thirst appreciation. *Clin Endocrinol* 1998; 49: 139 – 152.

35. Adrogue JH. Consequence of inadequate management of hyponatremia. *Am J Nephrol* 2005; 25: 240 – 249.

36. Bankir L, Bouby N, TArinh-trang-tan MM. The role of the kidney in the maintenance of water balance. *Clin Endocrinol Metab* 1989; 3-229:311.

37. Knepper MA, Gamba G. Urine concentration and dilution. Brenner and Rector's. *The Kidney, 7th Edition*, WB Saunders Company, Philadelphia 2004; 599 – 636.

38. Kokko JP, Rectore FC Jr. Countercurrent multiplication system without active transport in inner medulla: new model. *Kidney Int* 1972; 2: 214 – 23.

39. Nielsen S, Agre P. The aquaporin family of water channels in kidney. *Kidney Int* 1995; 48: 1057 – 68.

40. Nielson S, Kwon TH, Christensen BM, Promeneur D, Fronkiaer J, Marples D. Physiology and patho-physiology of renal aquaporins. *J Am Soc Nephrol* 1999; 10: 647 – 63.

41. Yamamoto T, Sasaki S. Aquaporins in the kidney emerging new aspects. *Kidney Int* 1998; 54: 1041 – 51.

42. Knepper MA, Wade JB, Terries J, Ecelbarger CA, Marples D, Mandon B et al. Renal aquaporins. *Kidney Int* 1996; 49: 1712 – 7.

43. Cadnapaphornchai MA, Schrier WR. Pathogenesis and management of hyponatremia. *Am J Med* 2000; 109: 688 – 692.

44. Nonoguchi H, Sands JM, Kneper MA. Atrial natriuretic factor inhibits vasopressin stimulated osmotic water permeability in rat inner medullary collecting duct. *J Clin Invest* 1988; 82: 1383 – 90.

45. Mandell IN, De Fronza RA Robertson GL, Forrest JN. Role of plasma vasopressin in the impaired water dieresis of isolated glucocorticoid deficiency in the rat. *Kidney Int* 1980; 17: 186 – 95.

46. Elalouf JM, Sari DC, de Rouffignac C. Effects of glucagons and the parathyroid hormone on the loop of Henle of rat juxta-medullary nephrons. *Kidney Int* 1986; 29: 807 – 13.

47. Carney S, Morgan T, Ray C, Thompson L. Effect of calcitonin on urine concentration in the rat. *Am J Physiol* 1983; 244: F432 – 5.

48. Beck TR, Dunn MJ. The relationship of vasopressin and renal prostaglandins. Miner Electrolyte Metab 1981; 6: 46 – 59.

49. Berl T, Verbalis J. Pathophysiology of water metabolism. Brenner and Rector's, *The Kidney, 7th edition*, WB Saunders Company, Philadelphia 2004; 857 – 919.

50. Man S. Management of hyponatremia and clinical use of vasopressin antagonists. *Am J Med Sci* 2007; 333(2): 101 – 105.

51. Goh KP, Management of Hyponatremia. *Am Fam Physician* 2004; 69: 2387 – 94.

52. Landnson JH, Apple FS, Koch DD. Misleading hyponatremia due to hyperlipidemia; a method dependent error. *Ann Int Med* 1981; 95: 707 -8.

53. Mass AHJ, Siggaard-Andersen O, Weisberg HF, Zijlstra WG. Ion-selective electrodes for sodium and potassium: a new problem of what is measured and what should be reported. *Clin Chem* 1985; 31:482 – 5.

54. Friedman E, Shadel M, Halkin H, Farfel Z. Thiazide induced hyponatremia; reproducibility of single dose rechallenge and an analysis of pathogenesis. *Ann Intern Med* 1989; 110: 24 – 30.

55. Fichmann MP, Vorrherr H, Kleeman CR, Telfer N. Diuretic induced hyponatremia. *Ann Intern Med* 1971; 75: 853 – 63.

56. Sonnenblick M, Friedlander Y, Rosin a. Diuretic induced hyponatremia. *Chest* 1993; 103: 601 – 6.

57. Boykin J, de torrnte A, Robertson GI, Erickson A, Schrier RW. Persistent plasma vasopressin levels in hypoosmolar state associated with mineralocorticoid deficiency. Miner Electrolytes Metab 1979; 2:310 – 15.

58. Eters JP, Welt LG, Sims EAH, Orloff J, Needham J. A salt wasting syndrome associated with cerebral disease. *Trans Assoc Am Physicians* 1950; 63: 57 – 64.

59. Harrigan MR. Cerebral salt wasting. *Crit Care Clin* 2001; 17: 125 – 38.

60. Harrigan MR. Cerebral Salt wasting syndrome: A review. *Neurosurgery* 1996; 38: 152 – 60.

61. Damraju SC, Rajshekar V, Chandy MJ. Validation study of a central venous pressure based protocol for the management of neurosurgical patients with hyponatremia and natruresis. *Neurosurgery* 1997; 40: 312 – 7.

62. Adrogue HJ, Madias NE. Hyponatremia. *N Engl J Med* 2000; 342: 1581 – 1589.

63. Jillier TA, Abbtt RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. *Am J Med* 1999; 106: 399 – 403.

64. Silver SM, Kozlowki SA, Baser JE, Rogers SJ, Sterns RH. Glycine induced hyponatremia in the rat a model of post prostatectomy syndrome. *Kidney Int* 1995; 47: 262 – 8.

65. Istre O, Bjoennes J, Naess R, Hornback K, Forman A. Post operative cerebral edema after transcervical endometrial resection and uterine irrigation with 1.5% glycine. *Lancet* 1994; 344: 1187 – 9.

66. Smith DM, Me Kenna K, Thompson CJ. Hyponatremia. *Clin Endoicrinol* 2000; 52: 667 – 78.

67. George JM, Capen CC, Philips AS. Biosynthesis of vasopressin in vitro and ultra structure of bronchogenic cancer. *J Clin Invest* 1972; 5: 141 – 8.

68. Robertson GL. Syndrome of inappropriate dieresis. *N Engl J Med* 1989; 321: 538 – 9.

69. Smith D, Moore K, Tormey W, Baylis PH, Thompson CJ. Downward resetting of the osmotic threshold for thirst in patients with SIADH. *Am J Physiol Endocrinol Metab* 2004; 287: E1019 – E1023.

70. Skowsky WR, Kikuchi TA. The role of vasopressin in the impaired water excretion of myxedema. *Am J Med* 1978; 64: 613.

71. Iwasaki Y, Oiso Y, Yamanouchi K. Osmoregulation of plasma vasopressin in myxedema. *J Clin Endocrinol Metab* 1990; 70: 534 – 9.

72. Oelkers W. Hyponatremia and inappropriate secretion of antidiuretic hormone in patients with hypopituitarism. *N Engl J Med* 1989; 321: 492 – 6.

73. Green HH, Harrington AR, Valtin H. On the role of antidiuretic hormone in the inhibition of acute water dieresis in adrenal insufficiency and the effects of gluco and mineralocorticoids in revising the inhibition. *J Clin Invest* 1970; 49:1724 – 36.

74. Riggs AT, Dysken MW, Kim SW, Opsahl JA. Reviews of disorders of water homeostasis in psychiatric patients. *Psychosomatics* 1991; 32: 133 – 48.

75. Goldman MB, Luchins DJ, Robertson GL. Mechanisms of altered water metabolism in psychotic patients with polydispsia and hyponatremia. *N Engl J Med* 1998; 20: 773 – 81.

76. Coenraad MJ, Bolk JH, Frolich M, Meinders AE. Plasma arginine vasopressin and arterial natriuretic peptide concentration in patients with

hyponatremia at diagnosis and following treatment. *European Journal of Internal Medicine* 2007; 18: 221 – 229.

77. Schrier RW, Fassett RG. Pathogenesis of sodium and water retention in cardiac failure. *Renal Failure* 1998; 20: 387 – 403.

78. Schrier RW, Martin PY. Recent advances in the understanding of water metabolism in heart failure. *Adv Exp Med Biol* 1998; 449: 415 – 26.

79. Xu DL, Martin PY, Ohara M, St John J, Pattison T, Meng X et al. Upregulation of aquaporin water channel expression in chronic heart failure in rats. *J Clin Invest* 1997; 99(7): 1500 – 1505.

80. Boscoe A, Paramore C, Verbalis JG. Cost of illness of hyponatremia in the United States. Cost effectiveness and Resource Allocation 2006; 4:10.

81. Montain SJ, Sawka MN, Wenger CB. Hyponatremia associated with exercise: risk factors and pathogenesis. Exerc Sports Sci Rev 2001; 29(3): 113 – 117.

82. Fall PJ. Hyponatremia and hypernatremia: a systematic approach to causes and their correction; *Postgrad Med* 2005; 107(5): 75 – 82.

83. Schrier RW, Gross P, Gheorghiade M, Berl T, Verbalis JG, Czerwiec FS, Orlandi C. Tolvaptan, A selective Oral Vasopressin V(2) – Receptor Antagonist, for hyponatremia. *N Engl J Med* 2006; 355(20): 2009 – 112.

84. Rabinstein AA, Wijdicks EFM, Hyponatremia in critically ill neurological patients. *The Neurologist* 2003; 9:290 – 300.

85. Tripathi M, Sanjeev CC, Roy AK. Chasing Hyponatremia: Unusual Presentation. *Neurol India* 2001; 49: 197 – 199.

86. Goldberg A, Hammerman H, Petcherski S, Nassar, Zdorovyak A, Yalonetsky et al. Hyponatremia and Long-term Mortality in Survivors of Acute ST-elevation Myocardial Infarction. *Arch Intern Med* 2006; 166: 781 – 786.

87. Miyazaki T, Yamamura Y, Onogawa T, Nakamura S, Kinoshita S, Nakayama S et al. Therapeutic effects of tolvaptan, a potent, selective nonpeptide vasopressin V_2 receptor antagonist, in rats with acute and chronic severe hyponatremia. *Endocrinology* 2005; 146(7): 3037 – 3043.

88. Rajul L. Hyponatremia in neurological diseases in ICU. *Indian J Crit Care Med* 2005; 9: 47 – 51.

89. Arieff AI. Guisado R. Effects on the central nervous system of hypernatremic and hyponatremic states. *Kidney Int* 1976; 10: 104 – 16.

90. Cumming A, Plant W. Wate, electrolytes and acid-base balance. *Davidson's Principles and Practice of Medicine. 19th ed.* Churchill-Livingstone. Edinburgh 2002; 280 – 3.

91. M Yaqoob. Water, Electrolyte and acide-base balance. *Kumar and Clark's Clinical Medicine, 6th ed.* Churchill-Livingstone. Edinburgh 2005; 701 – 703.

92. Mattle H. Neurologic manifestations of osmolality disorders. *Schweiz Med Wochenshr* 1985; 115(26): L 772.

93. Sonnenshein CH, Nielsen AK, Engquist A. Cerebral symptoms in hyponatremia. Treatment and course. Ugeskr Laeger 1991; 15. 153(29): 2065 – 9.

94. Londner M, Carr CM, Kelen GD. Fluid and Electrolyte problems. *Emergency Medicine – A comprehensive guide, 5th ed.* McGraw Hill 2000; 153 – 6.

95. Defronzo RA, Arieff AI. Ch 8. Disorders of sodium metabolism. Fluid, electrolyte and acid base disorders. 2nd ed. Churchill Livingstone 1995: 277.

96. Orakzai RH, Orakzai SH, Hasley PB. Treating hyponatremia: How slow is safe? Central pontine myelinolysis despite appropriate correction of hyponatremia. *Eur J Intern Med* 2008; 1 – 3.

97. Gullans SR, Verbalis JG. Control of brain volume during hyperosmolar and hypoosmolar conditions. *Ann Rev Med* 1993; 44: 289 – 301.

98. Schrier R. The patient with hyponatremia or hypernatremia. *Manual of Nephrology*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2000: 21 – 36.

99. Mulloy AL, Caruana RJ. Hyponatremia emergencies. *Med Clin North Am* 1995;

79(1): 155 – 68.

100. Miller M. Morley JE. Rubenstein LZ. Hyponatremia in a nursing home population. *J Am Geriatr Soc* 1995; 43(12): 1410 – 3.

101. Misra SC, Mansharamani GG. Hyponatremia in elderly hospital in-patients. *Br J Clin Pract* 1989; 43(8): 295 – 6.

102. Goldenstein. Idiopathi SIADH possible to advancing age. *Ann Intern Med* 1983; 99: 185 – 8.

103. Hochman I, Cabili S, Peer G. Hyponatremia in internal medicine ward patients: cause, treatment and prognosis. *Isr J Med Sci* 1989; 25: 73 – 6.

104. Vurgese TA,Radakrishnan ,Mapkar .Frequency and etiology of hyponatremia in adult hospitalised patients in medical wards of a general hospital in Kuwait.kuwait medical journal 2006:38(3):211-213

PROFORMA

Incidence & etiology of hyponatremia

S.No IP No. Name:

Age Sex DOA DOD

Weight

Primary diagnosis:

SYMPTOMS

S.No.	Symptoms	Status		Duration
1	Nausea	Y	N	
2	Vomiting	Y	N	
3	Headache	Y	N	
4	Altered Mental Status	Y	N	
5	Hiccups	Y	N	
6	Seizures	Y	N	
7	Others	Y	N	

If others, please specify

Diet Habits:

Fluid intake:

Decreased intake:

MEDICAL HISTORY

S.No.	Co-morbid conditions	Status		Duration	Specify
1	Diabetes Mellitus	Y	N		
2	Hypertension	Y	N		
3	Cardiovascular	Y	N		
4	Renal Problems	Y	N		
5	Endocrine	Y	N		
6	Respiratory	Y	N		
7	Neurological	Y	N		
8	Gasterointestinal	Y	N		
9	Others	Y	N		

If others, please specify

CURRENT MEDICATIONS

S.No.	Drug Name	Duration	Dosage/day	Causes Hyponatremia	
1				Y	N
2					
3					
4					
5					
6					

CLINICAL FINDINGS

Pulse Rate / min. Blood Pressure mmHg

Volume status at the time of admission: Hypovolemic / Hypervolemic / Euvolemic

Oedema: Y / N Ascites / Pedaledema

Dehydration: Y / N

BIOCHEMICAL PARAMETERS (At the time of admission)

Serum sodium level: Urine spot sodium:

Serum osmolality: Urine osmolality:

Na Urea Glucose

Random Serum Cortisol: Done / Not done Random serum cortisol level:

ACTH stimulation test:

TFT: Done / Not done TSH: Free T4:

Calculated sodium deficit: Diuretics Y / N

Infusion Plan: Fluid restriction Y / N

Specific drugs

Outcome: Asymptomatic / Symptomatically better / Same status

Discharged / Death / AMA / Transfer

Hyponatremia Cause

Possible secondary cause

Formula

Calculated serum osmolality: 2 x Na + Glu / 18 + Urea/6

ABBREVIATIONS

- ADH : Antidiuretic hormone
- AIDS : Acquired Immuno Deficiency Syndrome
- ANOVA : Analysis of variance
- ARC : Aids-related Complex
- ATPase : Adenosine Triphosphatase
- AVP : Arginine vasopressin
- C : Centigrade
- cAMP : Cyclic adenosine monophosphate
- Cl : Chloride
- COPD : Chronic Obstructive Pulmonary Disease
- CO_3 : Carbonate
- Dl : Deciliter
- FE : Fractional Excretion
- G : Gram
- GFR : Glomerular Filtration Rate

- H^+ : Hydrogen ion
- H_2O_2 : Hydrogen peroxide
- H_2O : Water
- HCo3 : Bicarbonate
- HIV : Human Immunodeficiency virus
- hrs : Hours
- IHD : Ischemic Heart Disease
- ISE : Ion Selective Electrodes
- K^+ : Potassium
- Kg : Kilogram
- L : Litre
- MDMA : 3,4 Methylenedioxymethamphetamine
- mEq : Milliequivalents
- mg : Milligram
- Mmol : Millimoles
- m Osm : Milliosmoles

- N_2 : Nitrogen
- Na^+ : Sodium
- NAD^+ : Nucleotide Adenine Dinucleotide
- NAD(P) : Nucleotide Adenine Dinucleotide Phosphate
- ng : Nanogram
- NH_4^+ : Ammonium
- NSAID's : Non Steroidal Anti-inflammatory drugs
- O_2 : Oxygen
- Pg : Pictogram
- PTB : Pulmonary Tuberculosis
- SIADH : Syndrome of Inappropriate Antidiuretic Hormone
- SD : Standard Deviation
- % : Percentage
-

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE,CHENNAI-600 003.

Telephone : 25363970

Fax :044 – 253-5115
:044 25363970

L.Dis.No. 14597/ME5/ thicsDean/MMC/2009 Dated .09.2009

Title of the work : "Incidence & etiology hyponatremia in hospital patients"
Principal Investigator :
Department : Dr. G. Keshavashankar . P.G - M.D Obstetrical medicine Madras medical college - Ch-3.

The request for an approval from the Institutional Ethical Committee(IEC) was considered on the IEC meeting held on 23rd September 2009 at 2.00P.M. in Madras Medical College, Deans, Chamber, Chennai-3. / pharmacology seminar hall, madras medical college. Ch-3.

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The principal investigator and their term are directed to adhere the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
4. You should not deviate form the area of the work for which I applied for ethical clearnance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulations of the institution(s).
7. You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC,CHENNAI

CHAIRMAN
IEC MMC CHENNAI

DEAN
MADRAS MEDICAL COLLEGE
CHENNAI

Sl.No	Name	Age	Sex	Date of Admission	hypocalcemia in mmol	UR	CR@CL	Primary cause	secondary cause	chronic illness if any	DM	HT	CVA	RTA	Alcohol addiction	IF	others	Other causes hypocalcemia, if any	diuretics	sodium/ calcium	Pulse/Bp	Urine output/day	urine na in mEq/day	UFT	TFT	random urine sodium mEq/L (Na utilisation)	treatment	symptomatic/asymptomatic	cause of hypocalcemia	No. of cal sachets	outcome	urine urea/creatinine ratio
1	Suresh	60	M	7/31/08	Yes	Yes	Yes	BRONCHOPNEUMONIA/ Ca bronchus	No	Yes	No	No	Yes	No	No	No	No	No	euvolemic	119	105	74	612	240	Normal	Normal	Normal saline	symptomatic	SIADH	multi-factorial	improved	No
2	Sivananda	63	M	10/1/2008	Yes	Yes	No	DM nephropathy/LVF	No	Yes	No	Yes	Yes	No	Yes	No	No	No	hypervolemia	120	105	74	130	300	Normal	Normal	fixed rate diuretics	symptomatic	volume overload	single	improved	No
3	Rasi loganathan	60	M	1/31/08	Yes	Yes	No	brainstem stroke/CKD	Quadriparesis	Yes	No	Yes	No	No	No	No	No	No	aspiration pneumonia	No	No	Yes	hyp eu eulemia	119	126	120	No	270	Normal	Not done	Fixedrate	symptomatic	cerebral salt wasting syndrome/ CKD	multi-factorial	death	No
4	Dhanpal	75	M	2/01/08	Yes	Yes	No	CBS	Quadriparesis	Yes	No	Yes	Yes	No	Yes	Yes	No	No	No	euvolemic	120	120	80	180	251	Normal	Normal	Normal saline	asymptomatic	SIADH	single	improved	No
5	Ramanathan	60	M	2/01/08	Yes	Yes	Yes	CBS/A/DM	Hemiplegia/ paresis	Yes	No	Yes	Yes	No	No	No	Yes	No	acidosis	120	104	100	No	271	Normal	Not done	Normal saline	symptomatic	hypoglycemia	multi-factorial	improved	No
6	Lary anang ana	52	F	2/2/2008	Yes	Yes	No	AG/AADD	vomiting	Yes	No	Yes	No	No	No	No	diarrhea	dehydration	No	No	Yes	hyp eu eulemia	120	108	8	No	304	Not done	Not done	Normal saline	symptomatic	diarrhea	single	improved	No
7	Ramlooi	65	M	2/2/2008	Yes	Yes	No	hypoglycemia	No	Yes	No	Yes	No	Yes	Yes	No	No	No	euvolemic	121	123	No	110	322	No	Not done	Fixedrate Normal saline	asymptomatic	osmolality panacreatitis	single	improved	No
8	ayanchoudhuriam	65	M	2/2/2008	Yes	Yes	No	CKD, injuries, ad Hemorrhagic stroke/ Quadriparesis	Hemiplegia/ paresis	Yes	No	Yes	No	No	Yes	Yes	Yes	No	pleural effusion	No	No	Yes	hypervolemia	118	121	74	No	271	Normal	Not done	fixed rate diuretics	asymptomatic	volume overload	single	improved	No
9	aroop anvih	62	F	2/2/08	Yes	Yes	Yes	renal failure, AIDP,	quadriparesis	Yes	No	Yes	No	No	Yes	No	Yes	No	pyoderma	No	No	Yes	euvolemic	118	120	74	90	298	Normal	Normal	daily no fixed rate diuretics	asymptomatic	renal failure	single	improved	No
10	mhamed shafi	65	M	2/2/08	Yes	Yes	Yes	DCL/Hepatic encephalop athy	Dyscoloration	Yes	No	Yes	No	No	Yes	No	No	Yes	necrosis	No	No	Yes	hypervolemia	118	120	74	100	299	No	Not done	fixed rate diuretics	asymptomatic	multi-factorial renal failure	multi-factorial	death	No
11	sarvati	60	F	2/2/08	Yes	Yes	Yes	DM nephropathy/CKD	No	Yes	No	Yes	No	No	No	No	No	No	ascitis	Yes	No	Yes	hypervolemia	114	120	74	156	306	No	Not done	Fixedrate Renal artery stenosis	asymptomatic	volume overload	multi-factorial	not tolerated	No
12	ajesh	58	M	2/03/08	Yes	Yes	No	Addisons Disease	No	Yes	No	No	No	No	No	No	No	No	shock	No	No	Yes	euvolemic	125	105	74	150	263	Normal	Normal	Fixedrate	asymptomatic	Addisons disease	single	improved	No
13	Kanu	61	M	2/3/2008	Yes	Yes	Yes	cardiac failure	Yes	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	hyp eu eulemia	108	116	100	160	305	Normal	Normal	fixedrate	asymptomatic	volume overload	single	improved	No
14	Sukrpaul	69	M	4/3/2008	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	euvolemic	112	114	68	321	290	hypothyroid	Normal	fixedrate	asymptomatic	hypothyroidism	multi-factorial	improved	No
15	Ichia	57	F	4/3/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No	dyshpidemia	No	No	Yes	euvolemic	106	117	74	156	296	Normal	Normal	Fixedrate	asymptomatic	diuretic induced	multi-factorial	improved	No
16	manchij	65	M	4/03/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No	recent spine surgery	Yes	No	Yes	euvolemic	111	117	80	170	296	Normal	Normal	Fixedrate Other adrenal insufficiency	asymptomatic	adrenal insufficiency	single	improved	No
17	manila	70	F	5/03/08	Yes	Yes	No	AG/AADD	No	Yes	No	Yes	No	No	No	No	No	No	osteoporosis	No	No	Yes	euvolemic	120	120	74	242	275	Normal	Normal	Fixedrate	asymptomatic	SIADH	multi-factorial	improved	No
18	sankarshwarq ran	55	M	5/03/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	Yes	Yes	No	No	No	cerebral spondylosis	Yes	No	Yes	euvolemic	110	109	74	208	309	Normal	Normal	fixedrate	asymptomatic	diuretic induced	single	improved	No
19	srihari ian	67	M	5/8/2008	Yes	Yes	No	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	Yes	Yes	No	No	No	No	Yes	No	euvolemic	111	120	74	205	287	Normal	Normal	Fixedrate	asymptomatic	SIADH	single	improved	No
20	Singhsidhy ani	71	F	5/6/2008	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	euvolemic	113	117	80	412	295	Normal	Normal	Fixedrate Hydrocortisone	asymptomatic	SIADH	single	improved	No
21	ramavati	68	F	5/04/2008	Yes	Yes	Yes	cerebellar effusion	No	Yes	No	No	Yes	Yes	Yes	No	No	No	anemia	Yes	No	Yes	hypervolemia	116	123	84	262	280	Normal	Normal	diuretics	asymptomatic	fluid mal hypovolemia	single	improved	No
22	ufil	68	F	5/04/2008	Yes	Yes	No	acute infective cause	Yes	Yes	No	No	No	Yes	Yes	No	No	No	recent uti	Yes	No	Yes	euvolemic	123	102	70	195	308	Normal	Not done	Normal saline	symptomatic	advised pituatry work up	single	improved	No
23	balaram barvi	64	F	5/04/08	Yes	Yes	Yes	acute enrionary sy ndrome	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No	dyshpidemia	No	No	Yes	euvolemic	125	105	74	190	270	hypothyroid	Normal	No	asymptomatic	hypothyroidism	multi-factorial	improved	No
24	thandhuba	54	M	5/4/08	Yes	Yes	Yes	heat stroke	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	124	122	134	503	272	Normal	Not done	Nil	asymptomatic	fixedrate/ dehydration, hypothyroidism	multi-factorial	improved	No
25	chaney	68	F	5/5/2008	Yes	Yes	No	chronic diarrhea	No	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No	Yes	hyp eu eulemia	118	118	74	503	266	hypothyroid	Normal	Nil	asymptomatic	fixedrate/ dehydration, hypothyroidism	multi-factorial	improved	No
26	ayalakmi	67	F	5/5/2008	Yes	Yes	Yes	cardiac failure	No	Yes	No	No	Yes	No	Yes	No	No	No	No	Yes	No	Yes	hypervolemia	120	120	74	350	270	Normal	Normal	diuretics	asymptomatic	volume overload	multi-factorial	improved	No
27	subrahmanam	72	M	5/7/08	Yes	Yes	Yes	heat stroke	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	117	123	74	440	295	Normal	Normal	Nil	asymptomatic	fixedrate/ dehydration, hypothyroidism	single	improved	No
28	chatuirgajan	68	M	5/05/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	Yes	Yes	euvolemic	106	111	74	5669	290	Normal	Normal	5% saline	asymptomatic	hypothyroidism	single	improved	No
29	Krishnarachari	72	M	5/05/08	Yes	Yes	Yes	acute infective cause	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	102	74	406	270	hypothyroid	Normal	Nil	asymptomatic	hypothyroidism	multi-factorial	improved	No
30	mandrajan	72	M	5/6/2008	Yes	Yes	Yes	cardiac failure	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	106	114	74	690	305	Normal	Not done	diuretics	asymptomatic	volume overload	multi-factorial	improved	No
31	thellamai	65	F	5/6/2008	Yes	Yes	Yes	fracture C6-C7	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	108	117	74	220	300	Normal	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
32	Sivabarli	70	F	5/6/2008	Yes	Yes	Yes	hypothyroidism	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	117	74	345	295	Normal	Normal	Nil	asymptomatic	adrenal insufficiency	single	improved	No
33	muralidharan	69	M	5/08/2008	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	111	119	74	401	290	Normal	Normal	5% saline	asymptomatic	diuretic induced	single	death	No
34	sivbalamal	71	F	5/6/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	108	117	74	198	263	Normal	Normal	5% saline	asymptomatic	diuretic induced	multi-factorial	improved	No
35	sudhabai	72	F	5/08/08	Yes	Yes	Yes	cardiac failure	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	106	107	68	180	300	Not done	Not done	diuretics	asymptomatic	volume overload	single	improved	No
36	nanthamarai	65	F	5/5/08	Yes	Yes	Yes	uroids	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	114	120	74	280	253	Normal	Normal	Nil	asymptomatic	diuretic induced	single	improved	No
37	amanathan	68	M	5/7/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	120	74	340	295	Normal	Normal	Nil	asymptomatic	diuretic induced	single	improved	No
38	mandarajan	68	M	5/07/08	Yes	Yes	Yes	acute calculus/ cholecystitis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	No	No	Yes	hyp eu eulemia	122	105	74	265	263	Normal	Normal	Nil	asymptomatic	hypovolemia	single	improved	No
39	sarvati	70	F	5/07/08	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	124	114	74	589	305	Normal	Normal	Nil	asymptomatic	SIADH	single	improved	No
40	geetha	52	F	5/07/08	Yes	Yes	Yes	seizure disorder	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	117	102	136	585	276	Normal	Normal	Nil	asymptomatic	SIADH	single	improved	No
41	krishnamurthy	60	M	5/8/2008	Yes	Yes	Yes	chronic SDH	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	122	123	74	317	260	Normal	Normal	Nil	asymptomatic	SIADH	single	improved	No
42	rajan	74	M	5/8/2008	Yes	Yes	Yes	cardiac failure	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	120	74	210	278	hypothyroid	Not done	5% saline	asymptomatic	hypothyroidism, thyroid redux	multi-factorial	improved	No
43	pancy anasamy	72	M	5/8/2008	Yes	Yes	Yes	post ictal observation	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	euvolemic	120	124	74	172	305	Normal	Not done	Nil	asymptomatic	post obstructive diuresis	multi-factorial	improved	No
44	pancyanand	72	M	5/08/2008	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	123	120	136	474	276	Normal	Not done	Nil	asymptomatic	diuretic induced	multi-factorial	improved	No
45	amanany	68	M	5/08/08	Yes	Yes	Yes	renal failure	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	hypervolemia	118	123	84	190	260	Not done	Not done	diuretics	asymptomatic	renal failure	single	improved	No
46	jaidya	66	F	5/08/08	Yes	Yes	Yes	meningitis	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	euvolemic	110	104	113	320	271	Normal	Not done	Nil, 5% saline	asymptomatic	SIADH	multi-factorial	improved	No
47	Ramchandran	64	M	5/8/2008	Yes	Yes	Yes	liver abscess	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	euvolemic	110	122	113	310	280	Normal	Not done	Nil	asymptomatic	diuretic induced	multi-factorial	improved	No
48	kalmadhy	67	F	5/9/2008	Yes	Yes	Yes	hypothyroidism	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	120	124	74	308	305	hypothyroid	Same/low	Nil	asymptomatic	healthy population	multi-factorial	improved	No
49	pavkulamal	64	F	5/19/2008	Yes	Yes	No	chronic diarrhea	No	Yes	No	Yes	No	No	No	No	No	Yes	No	Yes	No	Yes	hyp eu eulemia	116	123	74	292	278	Normal	Normal	5%, 3% saline	asymptomatic	SIADH	multi-factorial	improved	No
50	krima	54	F	5/9/08	Yes	Yes	Yes	acute cystitis/pyelitis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	Yes	No	Yes	euvolemic	120	122	74	256	260	Normal	Not done	5%, 3% saline	asymptomatic	renal failure	single	improved	No
51	george	52	M	5/09/08	Yes	Yes	Yes	hypothyroidism	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	108	104	74	310	270	hypothyroid	Same/low	5% saline	asymptomatic	healthy population	multi-factorial	improved	No
52	Sivalaksh	72	F	5/09/08	Yes	Yes	Yes	meningioma	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	122	74	146	256	Normal	Normal	Nil	asymptomatic	diuretic induced	multi-factorial	improved	No
53	Amanambly	72	M	5/10/2008	Yes	Yes	Yes	meningitis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	124	74	160	305	Normal	Normal	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
54	sundaramy	67	M	5/10/2008	Yes	Yes	Yes	CBS	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	121	130	644	262	Normal	Normal	5% saline	asymptomatic	osmolality panacreatitis	single	improved	No
55	samathi	67	F	5/10/09	Yes	Yes	Yes	cardiac failure	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	118	123	74	225	260	Not done	Not done	diuretics	asymptomatic	volume overload	single	improved	No
56	anthonysamy	68	M	5/10/09	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	108	108	74	97	304	hypothyroid	Normal	5% saline	asymptomatic	hypothyroidism	single	improved	No
57	Ramchandran	64	M	5/10/09	Yes	Yes	Yes	liver abscess	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	euvolemic	110	122	113	420	285	Normal	Not done	Nil	asymptomatic	SIADH	multi-factorial	improved	No
58	Rajarajan	67	F	5/10/09	Yes	Yes	Yes	septic arthritis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	119	121	74	130	265	Normal	Normal	5% saline	asymptomatic	diuretic / SIADH	multi-factorial	improved	No
59	sarvathi	64	F	5/11/2009	Yes	Yes	Yes	paralytic oncoph/halopathy	No	No	No	Yes	Yes	No	No	No	No	No	No	Yes	Yes	Yes	euvolemic	114	120	74	173	270	Normal	Not done	Nil	asymptomatic	diuretic induced	multi-factorial	improved	No
60	krishnavan	70	F	5/17/2009	Yes	Yes	Yes	cerebrovascular ill	No	No	No	Yes	Yes	No	No	No	No	No	No	Yes	Yes	Yes	euvolemic	120	122	74	112	270	Normal	Normal	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
61	syed shaikh	68	M	5/11/2009	Yes	Yes	Yes	acute infective cause	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	120	118	74	517	264	Normal	Normal	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
62	Selvavani	68	F	5/11/09	Yes	Yes	Yes	biliary tuberculosis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	122	74	307	273	Normal	Normal	5% saline	asymptomatic	SIADH	single	improved	No
63	Pancyanbiwat	74	F	5/11/09	Yes	Yes	Yes	AG/AADD/ABF	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	116	120	74	277	271	Not done	Not done	5%, 3% saline	asymptomatic	hypovolemia	multi-factorial	death	No
64	Gnalingam	72	M	5/11/09	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	107	114	113	224	258	Normal	Not done	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
65	sasikumaran	68	M	5/12/2009	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	112	117	74	210	275	Normal	Not done	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
66	krishnamurthy	60	M	5/12/2009	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	105	117	74	210	262	hypothyroid	Not done	Nil	asymptomatic	hypothyroidism	single	improved	No
67	jaidya	66	F	5/12/2009	Yes	Yes	Yes	hypothyroidism	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	114	120	74	212	265	hypothyroid	Same/low	5% saline	asymptomatic	healthy population	multi-factorial	improved	No
68	Ravi	72	M	5/13/2009	Yes	Yes	Yes	young stroke	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	119	124	74	300	271	Normal	Same/low	5% saline	asymptomatic	adrenal insufficiency	single	improved	No
69	amanarthy	72	M	5/15/2009	Yes	Yes	Yes	empty/isocoxar sepsis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	109	117	320	276	Normal	Normal	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
70	geetha	52	F	5/17/2009	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	120	74	336	275	Normal	Not done	5% saline	asymptomatic	healthy population	multi-factorial	improved	No
71	sathy anang ana	68	F	5/21/2009	Yes	Yes	Yes	ical fever	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	108	116	74	425	270	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
72	Jagdishchan	72	M	5/21/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	122	74	118	272	hypothyroid	Normal	Nil	asymptomatic	hypothyroidism	multi-factorial	improved	No
73	Gurugesan	61	M	6/3/2010	Yes	Yes	Yes	ectorrenal fever	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	post partic rather	No	No	Yes	hyp eu eulemia	120	122	74	130	305	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
74	Jamuna	72	F	6/3/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	103	125	352	260	hypothyroid	Not done	Nil	asymptomatic	diuretic induced	multi-factorial	improved	No
75	Mohanan	72	M	6/3/2010	Yes	Yes	Yes	pneumonia	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	120	126	74	304	295	Normal	Normal	Nil	asymptomatic	SIADH	single	improved	No
76	Chinivasan	70	M	6/03/10	Yes	Yes	Yes	ical fever	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	117	119	74	215	300	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
77	Sankaran	72	M	6/3/2010	Yes	Yes	Yes	hypoglagic	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	114	122	74	178	280	Normal	Normal	Nil	asymptomatic	SIADH	single	improved	No
78	Selchoi	72	F	6/03/10	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	117	74	230	276	Normal	Not done	Nil	asymptomatic	SIADH	single	improved	No
79	Sathna	67	F	6/3/2010	Yes	Yes	Yes	pneumonia	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	126	104	68	114	276	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
80	Jaidya	66	F	6/3/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	126	68	336	275	Normal	Not done	5% saline	asymptomatic	SIADH	single	improved	No
81	gopal	68	M	6/3/2010	Yes	Yes	Yes	ical fever	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	108	118	74	117	260	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
82	Sivalaksh	72	F	6/3/2010	Yes	Yes	Yes	cardiac failure	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	118	123	74	273	265	Not done	Not done	diuretics	asymptomatic	volume overload	single	improved	No
83	Anantha	65	F	6/3/10	Yes	Yes	Yes	cardiac failure	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	120	120	74	273	270	Not done	Not done	5% saline	asymptomatic	volume overload	single	improved	No
84	mandarajan	72	M	6/3/10	Yes	Yes	Yes	acute infective cause	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	116	119	92	443	260	hypothyroid	Not done	5% saline	asymptomatic	hypothyroidism	single	improved	No
85	sanyath	72	M	6/03/10	Yes	Yes	Yes	ical fever	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	122	122	74	205	305	Not done	Not done	Nil	asymptomatic	diuretic induced	single	improved	No
86	subashini	64	F	6/3/2010	Yes	Yes	Yes	cardiac failure	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	116	120	74	371	264	Not done	Not done	fluid restriction	asymptomatic	volume overload	single	improved	No
87	Ramesh rao	72	M	6/3/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	122	74	380	270	Normal	Normal	5% saline	asymptomatic	SIADH	multi-factorial	improved	No
88	Sundhou	72	M	6/3/2010	Yes	Yes	Yes	seizure disorder	Yes	Yes	No	Yes	No	No	Yes	No	No	No	BPH	Yes	No	Yes	euvolemic	108	118	74	361	270	Not done	Not done	Nil	asymptomatic	diuretic induced	single	improved	No
89	Samalam	70	F	6/4/10	Yes	Yes	Yes	septic shock	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Vits	No	Yes	Yes	hyp eu eulemia	106	116	117	436	268	Not done	Same/low	Nil	asymptomatic	adrenal insufficiency	multi-factorial	death	No
90	Subbiah	72	M	6/3/10	Yes	Yes	Yes	hypothyroidism	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	120	74	-	280	hypothyroid	Same/low	5% saline	asymptomatic	healthy population	single	improved	No
91	samanmy	68	M	6/3/10	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	p-sy-chiatric	No	No	Yes	euvolemic	118	116	68	177	268	hypothyroid	Not done	5% saline	asymptomatic	hypothyroidism	multi-factorial	improved	No
92	Ramamurthi	72	M	6/4/2010	Yes	Yes	Yes	cardiac failure	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	122	74	662	265	Not done	Not done	diuretics	asymptomatic	volume overload	single	improved	No
93	Parsand	61	F	6/4/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	ano	Yes	No	Yes	euvolemic	120	120	74	245	305	Normal	Normal	Nil	asymptomatic	SIADH	multi-factorial	improved	No
94	Sabir	77	M	6/4/10	Yes	Yes	Yes	acute bronchitis	Yes	Yes	No	Yes	No	No	Yes	No	No	No	ca prostate	Yes	No	Yes	hyp eu eulemia	120	125	113	280	262	Normal	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
95	Sivaraj samy	72	M	6/4/10	Yes	Yes	Yes	DCL/Hepatic encephalop athy	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hypervolemia	120	122	84	230	265	Not done	Not done	diuretics	asymptomatic	liver failure, renal failure	multi-factorial	death	No
96	sriram	68	M	6/04/10	Yes	Yes	Yes	NGE	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	hyp eu eulemia	110	102	84	220	264	Not done	Not done	Nil	asymptomatic	hypovolemia	single	improved	No
97	Sala	72	F	6/5/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	114	120	74	270	276	Not done	Not done	Nil	asymptomatic	diuretic induced	single	improved	No
98	Ramaraja an	67	M	6/5/2010	Yes	Yes	Yes	paralytic oncoph/halopathy	Yes	Yes	No	Yes	No	No	Yes	No	No	No	BPH	Yes	No	Yes	euvolemic	118	120	74	250	273	Not done	Not done	Nil	asymptomatic	diuretic induced	single	improved	No
99	Sankaran	68	M	6/5/10	Yes	Yes	Yes	acute infective cause	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	112	117	68	95	276	Normal	Same/low	5% saline	asymptomatic	adrenal insufficiency	single	improved	No
100	Kamal	70	M	6/5/10	Yes	Yes	Yes	RTA, neurosurg pneumonia	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	euvolemic	120	117	68	90	250	Normal	Not done	5% saline	asymptomatic	SIADH	multi-factorial	improved	No